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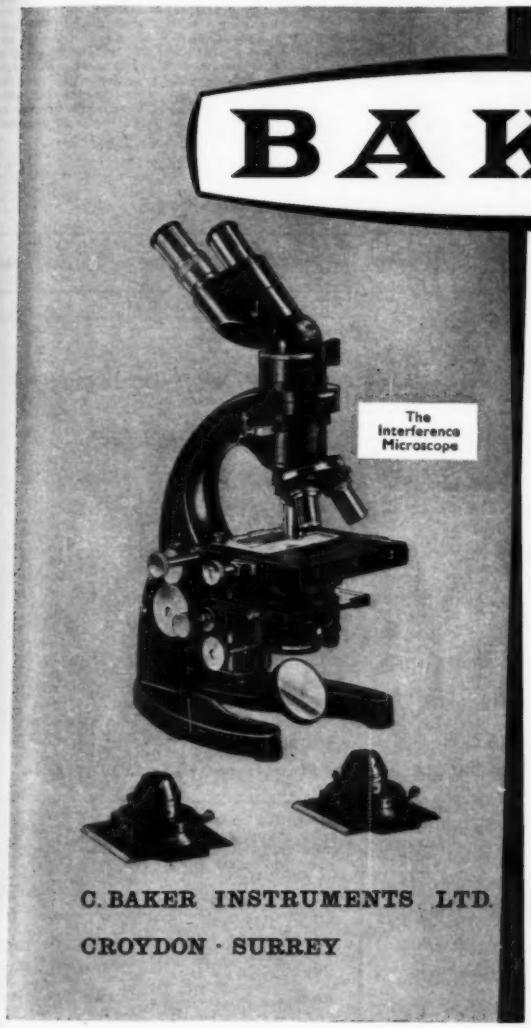


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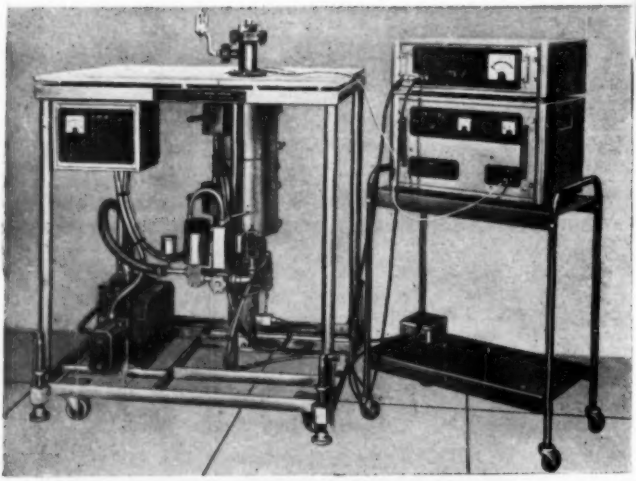

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# NATURE

No. 4756 SATURDAY, DECEMBER 24, 1960 Vol. 188

## CONTENTS

| | Page |
|---|---|
| Industrial Research and Development | 1055 |
| The Newer Cosmology. By Prof. Herbert Dingle | 1058 |
| Space Research. By D. G. King-Hele | 1058 |
| Invariance Properties of Particles and Fields. By Dr. A. Ashmore | 1059 |
| Chemicals and Insects. By Dr. W. A. L. David | 1059 |
| Control of Plant Growth. By Dr. D. J. Watson | 1060 |
| Early Thoughts on Progress and Profits. By Prof. S. G. Checkland | 1060 |
| Tungsten-185 from Nuclear Bomb Tests as a Tracer for Stratospheric Meteorology. By Dr. Herbert W. Feely and Prof. Jerome Spar | 1062 |
| Origin of the Pacific Basin: a Meteorite Impact Hypothesis. By E. R. Harrison | 1064 |
| Experiments with Diving Seals. By Prof. R. J. Harrison | 1068 |
| Obituaries: | |
| Dr. Hugh Scott, F.R.S. By E. B. Britton | 1070 |
| Dr. A. B. Edwards. By F. L. Stillwell | 1071 |
| News and Views | 1072 |
| City of Liverpool College of Technology. By S. A. J. Parsons | 1076 |
| Croydon Technical College | 1077 |
| Biology of Space Travel | 1078 |
| Influence of Climate on Life. By Dr. E. M. Glaser | 1080 |
| Colonial Development and Welfare | 1081 |
| Control of Infections | 1082 |
| Optical Image Assessment. By Dr. N. S. Kapany | 1083 |
| The Action of Nitrous Acid on Aliphatic Amines. By Dr. A. T. Austin | 1086 |
| Correlation of Biological Activity and the Electron Spin Resonance Signal Strength from Guinea Pig Adrenals. By Frank K. Truby and Dr. Joseph W. Goldzieher | 1088 |
| Theories of Shape Discrimination in *Octopus*. By Prof. J. A. Deutsch; Dr. N. S. Sutherland | 1090 |

(*Continued overleaf*)

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# LETTERS TO THE EDITORS


Page

PHYSICS

Pressure Dependence of Resistivity of Indium Antimonide to 70,000 Atmospheres.—H. A. Gebbie, P. L. Smith, I. G. Austin and J. H. King . . . . . 1095

Diffusion of Cadmium into Gallium Arsenide.—F. A. Cunnell and C. H. Gooch . . . 1096

Fine Structure of the Nuclear Magnetic Resonance Spectra of Solids: Chemical Shift Structure of the Spectrum of Phosphorus Pentachloride.—Prof. E. R. Andrew, A. Bradbury, Dr. R. G. Eades and G. J. Jenks . . . 1096

Line Breadths in the Ammonia Spectrum.—J. A. Fulford . . . . . 1097

Sustained, Localized, Pulsed-Microwave Discharge in Air.—Charles W. Hamilton . . . 1098

CRYSTALLOGRAPHY

Crystal Structure of $Ba_{2-x}TaO_{3-x}$.—Francis Galasso and Prof. Lewis Katz . . . 1099

GEOLOGY

Spectral Reflectivity of Ore Minerals.—I. Gray and Dr. A. P. Millman . . . . . 1100

GEOCHEMISTRY

Pigments of a Fossil Echinoderm.—Dr. Max Blumer . . . . . 1100

Exposure Ages for Iron Meteorites.—Dr. H. Wänke; Dr. Oliver A. Schaeffer . . . 1101

CHEMISTRY

Crystal Structures of 1-Chloro-2,4-Dinitrobenzene and 1-Bromo-2,4-Dinitrobenzene.—K. J. Watson . . . . . 1102

Magnetic Resonance of Protons in Glasses.—D. Elwell, D. Kumar and Dr. D. Williams . . 1103

Atomic Polarizations of Chloro-, Bromo- and Iodo-benzene.—Dr. H. H. Huang and Dr. E. P. A. Sullivan . . . . . 1104

Ionic Conductances in Gels of Wheat Starch.—Dr. Roger Collison . . . . . 1105

BIOCHEMISTRY

Structure of *Iso*metamidium (M. and B. 4180*A*), 7-*m*-Amidinophenyldiazoamino-2-amino-10-ethyl-9-phenylphenanthridinium Chloride Hydrochloride, the Red Isomer present in Metamidium.—S. S. Berg . . . . . 1106

1,3-Dialkyl-6-thioxanthines: a New Series of Bronchodilators and Coronary Vasodilators.—A. K. Armitage and K. R. H. Wooldridge . 1107

Ayapin, Scopoletin and 6,7-Dimethoxycoumarin from *Dendrobium thyrsiflorum* (Reichb. f.).—T. C. Wrigley . . . . . 1108

Reserpine Analogues.—Dr. T. Kralt, H. D. Moed, V. Claassen, Th. W. J. Hendriksen, A. Lindner, H. Selzer, F. Brücke, G. Hertting and G. Gogolak . . . . . 1108

Effects of Short-term Weaning on the Acid-soluble Ribonucleotides of Rat Mammary Gland.—D. Y. Wang . . . . . 1109

Reduction of α-Ketobutyrate by Human Serum.—Dr. S. B. Rosalki and Dr. J. H. Wilkinson . 1110

Composition of the Free Fatty Acid Fraction in the Plasma of Human Arterial Blood.—C. Chlouverakis and Dr. Peter Harris . . 1111

A New Cyclic Dipeptide from Peptone.—Prof. Takuo Kosuge and Hiroko Kamiya . . 1112

Stabilization of Thymidylate Kinase Activity by Thymidylate and by Thymidine.—Dr. Tadeusz B. Bojarski and Howard H. Hiatt . . 1112

PHYSIOLOGY

Specificity of the Effects of Cardiac Glycosides on the Rhythmic Contraction of Single Cultured Cardiac Muscle Cells.—Prof. Albert Wollenberger and Willi Halle . . . . . 1114

Page

Adrenaline and Blood Lipids.—Dr. A. N. Graitsas, E. D. Kuvelas and A. Konstantopulos . 1115

Catalase Activity of Mouse Liver and its Relation to the Condition of the Animal.—Dr. K. G. van Senden and J. de Jong . . . . 1116

Toxicity of a Single Subcutaneous Dose of Sodium Selenite in Pigs.—Kerstin Orstadius . 1117

Effects of γ-Aminobutyric Acid and Picrotoxin on Spontaneous Activity in the Central Nervous System of the Crayfish.—Prof. Joseph K. Hichar . . . . . 1117

Incorporation of Amino-Acids labelled with Carbon-14 in Nerve Proteins during Activity and Recovery.—Mario Luxoro . . . . 1119

Hydroxyproline and the Shrinkage Temperature of Collagen.—Dr. J. H. Bowes and Dr. J. A. Moss; Dr. B. J. Rigby and Dr. J. D. Spikes . 1120

HÆMATOLOGY

Possible Origins of the Anti-Gm Sera.—C. Ropartz, J. Lenoir, Y. Hemet and L. Rivat . . . 1120

Thalassæmia in a Tibetan discovered during a Hæmoglobin Survey among the Sherpas.—F. S. Jackson, Dr. H. Lehmann and Dr. A. Sharih . 1121

HISTOLOGY

Neurokeratin Network of Myelin Sheaths.—Prof. M. A. MacConaill and E. Gurr . . . . 1122

Structure of the Walls of the Bile 'Canaliculi' in Mammalian Liver Cells.—J. M. Davis . . 1123

PATHOLOGY

Porphyrin Fluorescence of experimentally produced Squamous Cell Carcinoma.—Dr. F. N. Ghadially and W. J. P. Neish . . . . 1124

Phenylketonuria in Infant Monkeys.—Prof. Harry A. Waisman, Hwa L. Wang, Gail Palmer and Prof. Harry F. Harlow . . . . . 1124

RADIOBIOLOGY

Early Incorporation of Sulphur-35 Sodium Sulphate into Plasma Proteins of Man.—Dr. Bernard A. Sachs, Edward Siegel and Joseph V. Marino . . . . . 1125

BIOLOGY

Sun Navigation by Birds.—Prof. R. J. Pumphrey, F.R.S.; C. J. Pennycuick . . . . 1127

Reactions of Soil Nematodes to Coal-Tar Dyes.—Prof. John P. Hollis . . . . . 1128

Toxicity of Aluminium to Black Pepper (*Piper nigrum* L.) in Sarawak.—P. W. F. de Waard and C. D. Sutton . . . . . 1129

Digestion of the Alga, *Macrocystis pyrifera*, by the Sea Urchin, *Strongylocentrotus purpuratus*.—Reuben Lasker and Richard A. Boolootian . 1130

Biosynthesis of Arbutin from Some Phenylpropanoid Compounds in *Pyrus communis*.—Prof. Sara K. Grisdale and Prof. G. H. N. Towers . 1130

ENTOMOLOGY

A Tick infesting the Nostrils of Man.—Dr. G. A. Walton . . . . . 1131

Atypical Spermiogenesis in *Thermobia domestica*, a Thysanuran Insect.—Dr. S. R. Bawa . . 1132

BACTERIOLOGY

Germination of Bacterial Spores by Long-Chain Alkyl Amines.—L. J. Rode and J. W. Foster 1132

VIROLOGY

Polyoma Virus in Syrian Hamsters: a Non-communicable Infection.—Prof. Bernard Roizman and Philip R. Roane, jun. . . . . 1134

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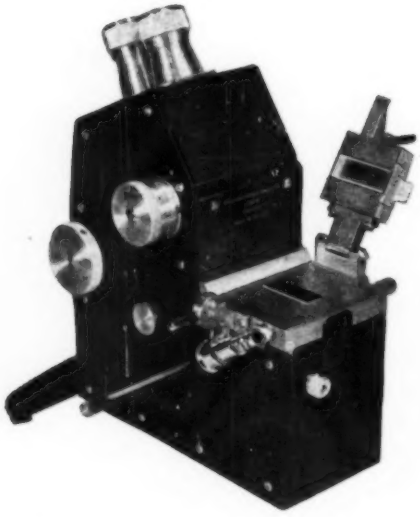

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# INDUSTRIAL RESEARCH AND DEVELOPMENT

IN the Sir David Russell Memorial Lecture delivered last March on the perils of leadership in science, Sir Lindor Brown said there are three major decisions of strategy to take in scientific work: what to start, when to stop, and where to go, in that rather peculiar order. Although Sir Harold Hartley's address* on the choice of subjects for research and development at the autumn research meeting of the Institution of Gas Engineers in November was concerned primarily with technology, his address recalled a good deal that Sir Lindor Brown said, as did indeed the debate opened by Lord Shackleton in the House of Lords on November 9 on the report of the Advisory Council on Scientific Policy. Lord Hailsham's important speech in that debate in particular indicated how largely the right balance of effort in the technological, as in the scientific, fields depends on wise decisions of exactly the type that Sir Lindor Brown emphasized. The prime requisite is always sound judgment.

Sir Harold Hartley, after quoting Prof. J. Jewkes's aphorism that science is directed towards understanding and technology towards use, and admitting that the economic aspects of research and development must always be governing criteria of policy, emphasized that the ultimate decision is always a matter of such judgment trained by experience. Moreover, like Lord Stamp, Sir Harold Hartley is well aware of the importance of suiting the tool to the job; Lord Stamp's observation that, while in writing a paper for the Royal Society 100 per cent accuracy is the objective, in industrial research a 60 per cent accuracy is a good achievement, is in line with Prof. T. L. Cottrell's recent criticism of the graduate's failure to apply theory or to approach a problem critically and consider the purpose to be served before choosing the means. Clearly what Sir Harold Hartley has in mind is the ability to seize an opportunity, and to make sound decisions as to what real openings may be offered by some interruption of a research programme through the demands of what he describes as first aid or an emergency call for immediate help.

Sir Harold is obviously prepared to accept a certain amount of such work as a legitimate function for a research department, provided that a careful watch is kept for such opportunities of new developments. Apart from this, it may lead to the acquisition of experience on which sound judgment can be based; this is not less true of work directed at the improvement of existing practices and products. Here he recognizes that the selection of research projects and the guidance of their progress are matters of national importance, and that it is not easy to determine the division of effort between the development of existing practices and exploring the possibilities of entirely new departures. One function of research in regard to the former is the provision of accurate and simple means for assessing efficiency; but this can tell us nothing about entering entirely new fields. On the other hand, the considerations and criteria that could be applied in assigning priorities to possible research projects, which Sir Harold described in this section of his paper, seem to be responsible for the continued demand manifested both in the House of Lords and in the House of Commons for the release of more information on such topics as the reports on shipbuilding research and on the machine-tool industry in Britain. It should also be added that in his reference to operational research into maintenance costs and research into instrumentation and automatic control, Sir Harold touched on a field which it is recognized offers increasing opportunities for co-operation between firms and groups of firms, both nationally and on an international scale.

In discussing his third category of research and development projects, namely, those aimed at the invention and development of new techniques, new materials and new appliances, Sir Harold Hartley relies rather too closely on Prof. J. Jewkes's study in "The Sources of Invention", and does little to clarify the distinction between research and invention or the factors that contribute to inventiveness, or even the criteria that may guide the choice of projects for research and development. Indeed, he accepts it as axiomatic that the bulk of the work of most industrial research laboratories will be concerned with what he describes as first aid, and with the improvement and development of existing processes in the light of advances in scientific knowledge. The choice of the latter projects must rest on cost analysis, on market research, and judgment of their scientific and engineering possibilities, though to suggest that they must also rest on the research effort available is to contradict a remark Sir Harold made in opening his address: there is surely a time at which a project calls for an expansion in research staff to seize an opportunity. That at least is obvious from some of the case-histories of Prof. Jewkes which Sir Harold quotes.

Sir Harold's argument here seems essentially to stress the importance of such an inquiry as that undertaken by the Advisory Council on Scientific Policy at the request of the Minister for Science; but he rightly emphasizes the need to adjust a research programme from time to time in accordance with its progress and other circumstances, and the importance in the direction and administration of research of an intimate day-to-day contact with the individuals concerned so as to avoid frustration or the destruction of confidence. He also makes one important constructive suggestion. The most successful system he has seen involved detaching a group of able people

* Institution of Gas Engineers. Publication No. 578: The Choice of Subjects for Research and Development. By Sir Harold Hartley. Pp. 9. (London: Institution of Gas Engineers, 1960.)

from all responsibility for specific projects, so that they could follow the progress of the different projects and keep in close touch with both the makers and the users of the products of the laboratory. The group was thus in a position to adjust the research programme to meet changing circumstances, and it was on its advice that projects were strengthened if they showed promise and were needed, or slowed down, or stopped. Sir Harold recognizes that such a system requires delicate handling, but he said that it had worked well and prevented projects being continued long after they were likely to pay a dividend. It does not, however, appear to be a system that is easily applied to fundamental scientific research; but it is easily recognized as the embryo of the Advisory Council on Scientific Policy, as distinct from the research councils themselves. Lord Shackleton, who opened the debate in the House of Lords on November 9, appeared to recognize this, though he was not altogether willing to accept the division of function and responsibility between a research council and the Advisory Council for Scientific Policy. He seemed to lean too readily to the view that massive support of research is all that is required and to ignore the demands which the selection of projects makes for judgment. It is true that in discussing the magnitude of the research and development effort in Britain he recognized the need for further investigation, and particularly into comparative figures for expenditure in terms of the gross national product, but he was concerned as to whether the right balance was being maintained between research and development.

That balance was not really considered in the Advisory Council's recent report, which Lord Shackleton was discussing, but he did not suggest that the balance was necessarily wrong. He admitted that the distinction is difficult to draw in practice, and it could well be maintained that any survey of the scientific effort in Britain as a whole, such as the Advisory Council initiated, could not fail to bring to light any weaknesses, in either pure or applied science; indeed, the recent report directs attention to gaps quite impartially in the scientific and the technological field. Some of those gaps, as Lord Shackleton himself acknowledged, have been emphasized by Lord Hailsham, and two in particular received some emphasis in the debate. Both these were noted by Lord Shackleton, and Lord Hailsham, who followed him, referred to them in some detail. He began by stressing the importance which he and the Council attach to the reports of the Economic Section of the Council for Scientific and Industrial Research into the machine tools industry and into the shipbuilding industry. The purpose of these reports, which were concerned solely with the scientific and research aspects of these industries, was to keep the Advisory Council informed on the economic aspects of their scientific research and on their particular research programmes, so as to enable the Council to advise industry on what they may regard as their research requirements. In other words, the Economic Section is in large measure assisting the Advisory Council to fulfil one of the essential functions to which Sir Harold Hartley directed attention in his address to the Institution of Gas Engineers.

Lord Hailsham said that the report on the machine tools industry was compiled with the full co-operation of the industry and contained so much confidential information from individual firms that an undertaking had to be given that it would not be published without the consent of the industry itself. He believes that the report has already yielded important results. For example, it appeared that the pattern for training engineers in universities and colleges is not well suited to the needs of the machine tool industry, and in consequence of the report new courses are likely to be available. Also, it had established forcibly the need for a research association and one is already being formed. The need for development on certain lines had also been brought to light, and Lord Hailsham also referred to a forthcoming report from a committee under the chairmanship of Sir Stewart Mitchell appointed to consider Prof. Seymour Melman's report on the Western European machine tool industry presented to the European Productivity Agency last year.

This report was published on November 10, and afterwards the Department of Scientific and Industrial Research and the Machine Tools Trades Association issued a statement giving details of what is being done by way of schools of research, higher training in machine tool technology, scholarships and special courses, to meet the challenge to the British industry. Subsequent speakers in the debate again pressed Lord Hailsham on the publication of these two reports; but although he indicated that he had always favoured publication of such documents, he firmly defended the decision not to publish on the ground that a promise had been given in good faith that private information should be kept private. Nevertheless, it was clear that Lord Hailsham was much less happy about the report on the shipbuilding industry, and did not exclude the possibility of publication of that report or some modified version of it, or some programme of research which would embody part of the report. He stated originally that the information was not obtained on quite the same confidential basis as that in the report on the machine tool industry, and he did not regard the Department of Scientific and Industrial Research as having given an undertaking that the information should not be published. The decision whether or not the report should be published must rest with the Council for Scientific and Industrial Research; all that he urged was that the confidential discussions on which he was engaged with the industry should not be prejudiced by publication. On December 1, Sir David Eccles, as representing the Minister for Science, stated in the House of Commons that the industry and the Department had that morning agreed on publication as early as possible.

Two other comments made by Lord Shackleton drew important statements from the Minister for

Science. Lord Shackleton referred to the organization of Government research and the work of the Zuckerman Committee, and in reply Lord Hailsham outlined very clearly his conception of his own responsibilities. He proposed to use the Advisory Council on Scientific Policy as was indicated in its current annual report; but while the Government is responsible for seeing that gaps in our scientific activities are filled and the work is done, the responsibility for doing the work rests elsewhere—with the Research Councils, Government departments, the universities and industry. He is considering with the officers of the Royal Society how an even closer liaison could be achieved between that Society and the various bodies for which he is responsible.

In reply to Lord Shackleton's comment that some of the recommendations in the Advisory Council's report are too general, Lord Hailsham suggested that his function was to some extent discharged, in any event in the first degree, when he caused these questions to be asked; and that the right inference to be drawn was that the proposals are actively under discussion in independent fields as a result of the inquiry. Specifically, he agreed that the arrangement of the rapidly increasing work within the scope of the Research Councils requires further consideration; but as regards Lord Shackleton's request that he should entrust the responsibility for natural resources to the Nature Conservancy, he said that the Advisory Council on Scientific Policy would probably be asked to consider in the near future the detailed pattern of our effort in regard to natural resources.

On receiving the recent report, Lord Hailsham said he had directed the attention of the various responsible bodies to findings which he thought particularly concerned them. He was confident that the universities and the University Grants Committee would take the report into account, and though he fully recognized the force of the objection to earmarked grants, Lord Hailsham indicated that he would not hesitate to deal with the difficulty if need arose. He is particularly concerned at present, he said, both with the shortage of qualified engineers and with the insufficiency of engineering research, both in the universities and in industry. Both these factors are major weaknesses in Britain at present, and will not be removed until this field attracts a due proportion of the best intellects in the country.

Here Lord Hailsham suggested a decisive factor is the status which engineering enjoys in the universities, and this is a matter which only the universities can remedy. Lord Hailsham did hesitate to proclaim his own view that engineering should enjoy a far higher status in the universities than it has hitherto been allowed to do, and his profound respect for university autonomy should not be construed as inhibiting action if due regard is not paid to Britain's interests. Obviously, he prefers to work through the accepted channels, but the whole tenor of his speech implied readiness for resolute and even drastic action here and elsewhere if the need were established.

One other topic on which Lord Hailsham touched is the matter of development contracts. In 1952 the Advisory Council on Scientific Policy recommended that the use of development contracts in civil industry should be urgently explored, and afterwards the function of the National Research Development Corporation was extended to cover the promotion of research likely to lead to some important invention. The Department of Scientific and Industrial Research has been authorized to act as focus for the idea of civil development contracts; but so far results, apart from the activities of the Atomic Energy Authority and the National Research Development Corporation, have been meagre.

The Advisory Council takes the view that the problem of the development contract is not insoluble, though it is very difficult when Government is not the direct customer and has not laid down in detail the specifications and objectives; but a solution should substantially improve the development of the results of scientific research. It is not, however, in the Council's view, a problem to be solved by centralized action alone, but one in which industry must take a leading part. Essentially it is a matter of research-mindedness and a tradition of using the results of scientific and technological advance.

Lord Hailsham expressed the hope that this situation would soon be altered. He referred to proposals for development contracts in the field of machine tools likely to be put forward through the National Research Development Corporation or the Department of Scientific and Industrial Research, and to proposals under discussion for computers. It is possible that a new technique may be developed; but if this does not happen, it is clear that Lord Hailsham is prepared to examine the whole problem afresh, and in replying on the whole debate he made pointed and reassuring reference to the place of the research associations.

Neither the Advisory Council nor the Minister for Science is under any illusion that support of a research association is any substitute for research-mindedness and an active research policy within an individual firm; but both his speeches in this debate indicated that the Minister for Science, like the Advisory Council, has a firm grasp of essentials and of the conditions in which creative activity is most fruitful. Lord Hailsham revealed himself as determined to stimulate those conditions; but equally he was resolute to avoid generating unnecessary opposition or causing friction which might waste effort or defeat the objective. His final remarks that these matters should be kept clear of party politics so far as possible deserves to be widely noted. Emphatically, Lord Hailsham is right to hold that the relation between science and Government and between science and industry must be appropriate to the type of industrial and social organization a country possesses. All that should be added is that those relations should change as the organization may change, and without undue time lag. The provision of a Parliamentary Secretary to the Minister should assist the Minister for Science to pursue his inquiries into these and other matters

more readily and in greater detail. No scientist or technologist could well ask of a Minister for Science a more forward-looking mind than Lord Hailsham revealed in the debate, or clearer indication of readiness to act where necessary, while respecting the practices and traditions which have proved their value in scientific and academic work. He obviously looks to the research associations to play an important educational function in industry apart from any actual contribution to research, and the debate should dispose of any uneasiness as to the future of the research associations as a whole. Specifically, in reference to an instance mentioned by Lord Pethick-Lawrence, of a scientist who had left Britain for America because he was unable to obtain the equipment he needed here, Lord Hailsham undertook to examine any similar instance in which some particular aspect of science was not properly cared for by the provision of apparatus if the matter were brought to his notice. The keen awareness of the importance of scientific and technical education at all levels, and perhaps especially of that designed to provide the supporting technicians needed in the universities, as well as in industry and Government departments and institutions, was a most encouraging feature of a notable debate.

## THE NEWER COSMOLOGY

### The Nature of the Universe

By Prof. Fred Hoyle. New and extensively revised edition. Pp. vii+103+6 plates. (Oxford: Basil Blackwell, 1960.) 8*s*. 6*d*. net.

THIS is a revised edition of the well-known book of some ten years ago in which Prof. Hoyle recorded his very popular broadcast talks on what he described as "The New Cosmology". The order of presentation and general style are unchanged, but there are, of course, revisions of certain details. Chief interest, however, will centre on the substantial changes, and these are considerable.

The estimated density of interstellar matter has been reduced a thousandfold, thus annihilating important effects formerly ascribed to the 'tunneling' of stars through this medium. The number of planetary systems in a galaxy is now at least 1,000 and perhaps 100,000 times greater than before, while the age of our Galaxy, previously given as "quite definite and precise" is now increased fourfold and has become "reasonably definite and precise".

The greatest change, however, concerns the origin of the planets. In the earlier book it was shown that the idea that these originated from solar material "must be wrong", "hopelessly wrong", and that the planets "must have" originated in the explosion of a companion of the Sun. Now, however, it appears that the planets did originate from solar material, the companion having been non-existent. "There is no idle speculation here." Prof. Hoyle's faith that the cosmology of 500 years hence will appreciably resemble the particular cosmology of to-day which he now favours remains unshaken.

It is very remarkable that such fertile imagination and mathematical skill can accompany such credulity and lack of critical power in one person. The general reader may decide what weight to attach to the astronomical conjectures from the "personal view" at the end concerning "continued existence after death", for here he is not menaced by the fear of incommunicable mathematics in the background which elsewhere confounds his judgment. "My own answer would be that mind is an intricate organization of matter. In so far as the organization can be remembered and reproduced there is no such thing as death. If ordinary atoms of carbon, oxygen, hydrogen, nitrogen, etc., could be fitted together into exactly the structural organization of Homer, or of Titus Oates, then these individuals would come alive again exactly as they were originally. The whole issue therefore turns on whether our particular organization is remembered in some fashion. If it is, there is no death. If it is not, there is complete oblivion."

Suppose Prof. Hoyle were regrettably to die tomorrow, and someone fitted the atoms into the necessary structure: which view of the origin of planets would the resurrected mind, "as it was originally", take? If the structure changes from moment to moment while we live, to take account of growing experience, is it not strange that it never by accident gets shaken into a configuration that knows the future, and that so many otherwise quite diverse organizations all happen to be aware of the Suez crisis, say—now that it has occurred, of course? But perhaps, after all, our knowledge of these matters, as of some others, is not yet quite definite and precise.

HERBERT DINGLE

## SPACE RESEARCH

### The Exploration of Space

A Symposium on Space Physics, April 29–30, 1959. Edited by Robert Jastrow. (Sponsored by the National Academy of Sciences, the National Aeronautics and Space Administration, and the American Physical Society.) Pp. v+160. (New York and London: The Macmillan Company, New York, 1960.) 5.50 dollars; 38*s*. 6*d*.

THIS book is the record of the papers presented at the symposium on "Space Physics" held at Washington during April 1959, and of the 'round-table discussions' which concluded each session. The first three papers show how much has still to be learnt about interplanetary space, or the 'Sun's outer atmosphere' as it is now sometimes called. F. L. Whipple surveys our present knowledge of solid particles in the solar system, remarking that "the general subject of meteoritics is in a sorry plight". T. Gold deals with the ionized particles and magnetic fields, and stresses the importance of electromagnetic effects. E. Parker, looking at the same region with a different bias, emphasizes the hydrodynamic expansion of the solar corona, as it streams into space at speeds of around 500 km./sec. Next, the radiation zones are described by their discoverer, J. A. Van Allen, and the *Argus* experiment by its proposer, N. C. Christofilos. H. E. Newell reviews the United States plans for future space-vehicles, G. de Vaucouleurs summarizes what is known about Mars and Venus, and G. P. Kuiper discusses the Moon, contending that the craters are caused both by volcanic action and by meteoritic impacts. H. C. Urey, in a paper entitled "Primary and Secondary Objects", suggests that

stony meteorites originated in a primary object of roughly lunar size formed about 4,000 million years ago. There are two contributions concerned mainly with space-research techniques: H. Friedman on the rocket astronomy he has done so much to promote, and L. Goldberg on astronomy from satellites. Finally, J. W. Townsend outlines a programme for future space research, and R. Jastrow describes the Earth's outer atmosphere.

The book can be thoroughly recommended, and fully justifies the publishers' claim that it is a "comprehensive survey of the most recent developments in space science", though the developments are now not quite so recent as they were, since the increased pace of scientific progress has not been matched by any corresponding acceleration in printing, proof-reading —or reviewing. All but one of the papers given at the symposium were first printed in the November 1959 issue of the *Journal of Geophysical Research*, and the book is a faithful reproduction of the pages from the *Journal*, including all the misprints. The book illustrates a growing and deplorable tendency to reprint unchanged, in book form, scientific articles which are known to have misprints. If publishers wish to adopt this practice for economy, they should surely include a list of errata: for this book, such a list could well be headed by the value for the age of the Moon on page 143, which is in error by a factor of $10^{18}$.

D. G. KING-HELE

## INVARIANCE PROPERTIES OF PARTICLES AND FIELDS

### Theory of Elementary Particles

By Paul Roman. (Series in Physics.) Pp. xii+575. (Amsterdam: North-Holland Publishing Company; New York: Interscience Publishers, Inc., 1960.) 100*s*.

THE progress that has been made in establishing a basic theory of the elementary particles and their interactions has depended to a large extent on the use of invariance properties under transformations. These range from the obvious Lorentz transformations to rotations and reflexions in isobaric space. They give rise to conservation laws, selection rules and relationships between reactions, all of which can be tested by experiment. Their deduction does not necessitate the solution of the field equations, which has so far not proved to be generally possible for the strong interactions. For the weak interactions almost complete understanding has been achieved as a result of the comparatively recent discovery of the non-conservation of $P$ and $C$.

Dr. Roman's book is particularly concerned with the invariance properties and their influence on the structure of the quantum field theory used to describe the elementary particles and their interactions. The treatment is outstandingly good. It is inevitably mathematical and requires an effort on the part of the reader (particularly the experimental variety), as is recognized by the author in his preface. He has most successfully sugared the pill by setting out the mathematics in considerable detail and carefully discussing its implications and limitations. The experimental implications are kept constantly in view and it is made clear how experimental results have determined the structure of the theory at every stage.

The first 100 pages are devoted to the theory of the four-dimensional orthogonal group and its representations. In the next 114 pages the quantum field theory is developed, starting with a classical treatment of the field equations to establish their form for the different fields. Quantization of the fields is then introduced, leading to the commutation rules and the use of creation and annihilation operators. The remainder of the book is devoted to the invariance properties. In particular, $P$, $C$, $T$ transformations and the relation between them are considered in detail and a section is devoted to the effects of the non-conservation of $P$ and $C$ in weak interactions. Transformations in isobaric space are then introduced, leading to the Gell-Mann Nishijima classification of the elementary particles. There are interesting discussions of the $|\Delta t| = \frac{1}{2}$ selection rule and of the properties of neutral $K$ mesons. Finally, more complete mathematical models of the elementary particles are considered, including the Prentki–d'Espagnat theory of isospace. It should perhaps be mentioned that no attempt is made to include the methods (such as dispersion relations) that are being tried for dealing with the strong interactions.

This book can be recommended unhesitatingly to those who wish to become familiar with the basic theory of the elementary particles and their interactions. It will also be a vital source of reference for those who are only intermittently concerned with the basic aspects of the theory.

A. ASHMORE

## CHEMICALS AND INSECTS

### Methods of Testing Chemicals on Insects, Vol. 2.

Edited by Harold H. Shepard. Pp. iii+248. (Minneapolis, Minn.: Burgess Publishing Company; London: Mayflower Publishing Co., Ltd., 1960.) 40*s*.

THIS volume is the second in a series projected by the former Chemical-Biological Co-ordination Center, having as its object the publication of "a manual of test methods dealing with the effects of chemicals on insects".

The first volume has already been reviewed in *Nature* (**183**, 352; 1959). The second volume begins with a group of three papers: "Pre-test Conditions which affect Insect Reaction to Insecticides", "Factors affecting Insects during Exposure to Insecticides", and "Post-exposure Conditions and Determination of End Point". This division looks orderly on paper, but it is difficult to maintain, and a single chapter would probably have been preferable. Much of the second chapter would be more correctly entitled "Factors affecting Insecticides during the Exposure of Insects"—which is quite a different subject.

The remaining chapters deal with testing methods for insecticides used for specific purposes. Chapter 4, "Exposure to Treated Food Medium", and Chapter 5, "Screening Space Sprays against Flies and Cockroaches", give good straightforward outlines of the methods used, but some comments on the fundamental factors concerned would have assisted the intelligent use of these methods. Chapter 6 deals with "Soil Insecticides". Chapter 7, "Testing Resistance of Chemically Treated Textiles", unlike Chapter 5, gives full details for carrying out the tests, and it may be said again that it seems regrettable that the

various contributions are not standardized in this respect. Chapter 8, "Screening Chemical Repellents", describes various methods, and instructively relates the fundamentals of the subject to the testing procedure. Chapter 9 deals with "Insect Proofing of Food Packing Materials". Chapter 10, "Screening Chemical Attractants", gives a rather unorganized account of this difficult subject. It includes a method for assessing 'contact attractance' which is out of place, and much material about the use of attractants in conjunction with insecticides which has no relevance to screening.

Chapter 11, "Testing Acaricides", is one of the best in the book, and supplies the information that anyone embarking on this work would require. Chapter 12, a short one, entitled "Animal Sprays, Dusts, Dips and Dressings", gives an account of field test methods. Chapter 13, "Techniques for the Evaluation of Systemic Insecticides against Livestock Sprays", is a clear introduction to this subject. However, some of the methods used sound unpleasant for the animals, and one wonders if alternatives could not be devised.

This is a useful reference work and the best chapters give excellent introductions to the subjects discussed. Unfortunately test-insects are not listed in the index.

W. A. L. David

## CONTROL OF PLANT GROWTH

### Crop Production and Environment

By Dr. R. O. Whyte. New edition. Pp. 392+31 plates. (London: Faber and Faber, Ltd., 1960.) 63*s*. net.

THE title of this book is not a reliable guide to the contents. Some of the subjects discussed, for example, the morphology of stem apices, the biochemistry of reproduction and the effects of growth substances, extend into much wider fields than the relation between crops and their environment. On the other hand, the most important practical aspect of this relation—the dependence of crop yield on climate, seasonal weather and soil factors—is barely mentioned.

The purpose of the book is to summarize results of research on the physiology of plant growth and development published since 1946, when the first edition appeared, and to show their application in agriculture and horticulture. As in the first edition, the chief topic is control of morphological development, particularly flowering, by temperature and day-length, that is, vernalization and photoperiodism, but there is also some discussion of quantitative growth of field crops, and of the significance of leaf area as a determinant of yield. An account of equipment for growing plants in controlled environments ranges from commercial glasshouses to phytotrons. Twelve chapters deal with the physiology of growth of different crop species, and the "agricultural botanists, agronomists, crop ecologists, plant breeders and general biologists" for whom the book is intended will probably find this the more interesting and useful part.

The author's aim has been to give as much factual information as possible within the prescribed space; he has not attempted to write a critical review, nor to deduce general relationships from the mass of experimental data. The resulting narrative has no clear pattern and few connecting threads, so it is difficult to read and still more difficult to absorb. Much of the text consists of quotations from the original papers, and their variation in style contributes to the lack of unity and cohesion. The figures and plates are used to squeeze in still more information in a compact form; often they are not mentioned in the text, and sometimes the descriptions in the legends are inadequate.

Although, as the author himself says more than once, this book is superficial and not comprehensive, it will be a valuable reference work, for there is no other that attempts to cover the same ground. It is thoroughly documented, and has a bibliography of about four hundred references.

D. J. Watson

## EARLY THOUGHTS ON PROGRESS AND PROFITS

### Progress and Profits in British Economic Thought, 1650–1850.

By G. S. L. Tucker. (Cambridge Studies in Economic History.) Pp. vii+206. (Cambridge: At the University Press, 1960.) 27*s*. 6*d*. net.

MR. TUCKER provides a scholarly analysis of the course of the debate in Britain about the relationship between the return on investment and economic progress. It should be of great interest to those who ponder the attempts of societies to understand themselves.

It is a little curious that it is during the beginning of the story, in the second half of the seventeenth century, that the debate is closest to the kind of emphasis applied nowadays. For then men argued, more or less instinctively, about the ability of rulers to affect the course of events by manipulating an indicator, which might also be a determinant. Josiah Child and his kind were all for pushing down interest rates, to attain by synthetic means what the course of commerce had produced in Holland, with the idea that this would create the most favourable conditions for British commerce. But with Adam Smith, and especially Ricardo, the emphasis changed; the debate became more concerned with distribution than with growth. The author throws much light on how this occurred, though perhaps he does not sufficiently emphasize the restrictive nature of the full Ricardian theory, making the whole outcome depend on diminishing returns to agricultural effort. The only policy measure left to Ricardo and his school for the furthering of growth was the plea for free trade, so that the margin of cultivation could be thrown back to the New World. But with the next generation, though much Ricardian influence is still present, the problem of excessive capital formation has become pressing. Britain had arrived at a situation similar to that of the Dutch much earlier, but instead of plenty of capital guaranteeing progress, the fear that it might be excessive gains ground, as the stresses mount in Britain in the late 1830's and the 40's. Thus J. S. Mill, Wakefield, Torrens and others begin to think in terms of the export both of capital and men, so that both may find better opportunities abroad, and may, in conjunction, reduce the cost of imported primary products to Britain. Here, at the mid-nineteenth century, Dr. Tucker's story ends; he might well continue it.

S. G. Checkland

## Electrolytic Conductance

By Prof. Raymond M. Fuoss and Prof. Filippo Accascina. Pp. ix+279. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 59*s*.

THIS book deals with the theory of electrolytic conduction as developed on the basis of the Onsager equation by Fuoss and Kraus and later workers of their school. Briefly, their treatment was to introduce the Bjerrum hypothesis of the formation of ion pairs into the theory of Debye and Hückel, and to extend the treatment so as to cover non-aqueous solutions. In 1955, Fuoss and Onsager solved the theoretical problem for a model in which the ions were represented by charged spheres instead of point charges. The resulting equation involved two arbitrary constants, the limiting conductivity of the Onsager equation and the ion size. Fuoss later extended the treatment to electrolytes in which the ions are associated into ion pairs, but the equation is limited to very dilute solutions. The authors say in the preface that they do not think there is any hope of extending the theory to higher concentrations, where they think the treatment must start from fused salts, which are supposed to be diluted with non-electrolytic material.

The theory is developed in the book, the necessary mathematics being first summarized in short chapters on such matters as vectors and tensors (restricted to Gibbs's dyadics), hydrodynamics, and statistical mechanics. The static phenomena such as activity coefficients are fairly simply disposed of. The difficulty begins when conductivities are considered. The relaxation field is extended to higher terms, then binary and higher associations of ions are brought in. In general, the mathematical treatment is clearly set out, but it would be a help to the reader if it were stated at the beginning of each chapter just what was to be done in it. The book is restricted to the particular theory stated, but it contains material useful in the study of the alternative theories, which are not considered.

J. R. PARTINGTON

## The Physics of Electricity and Magnetism

By Prof. William Taussig Scott. Pp. xvi+635. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 70*s*. net.

ONE is conscious at the present time of the feed-back from research and discovery to the matter and methods of elementary instruction, or, more accurately perhaps, of the need for such a cycle. Physicists, for example, while complaining that the younger generation is ill-versed in the principles developed in the seventeenth and eighteenth centuries, also take exception to syllabuses and treatments that date from somewhere about the middle of the nineteenth. But it is not easy to see how to improve matters by any process of mere addition of information; substitution would be even less effective. The problem is one of integration, and the volume under review, though not elementary in standard, adopts this very refreshing approach with success.

Prof. Scott, after explaining the general ideas of charge, field, and potential in the first chapter goes on to the physics of the metallic state in the second and the behaviour of dielectrics in the third. By chapter seven, he is introducing the idea of the magnetic field in terms of the Lorentz law of force on a moving charge. The mathematical development, which is in itself ageless, is as firmly implanted in the pattern of modern physical thought as Maxwell's was in the physics of his day. The author claims that the book gives a sound logical basis for understanding the physics of electricity and magnetism, and this claim is justified. The level is about that of the honours degree.

G. R. NOAKES

## A Degree Physics

By Dr. C. J. Smith. Part 5: Electricity and Magnetism. Second edition. Pp. vii+743. (London: Edward Arnold (Publishers), Ltd., 1959.) 45*s*. net.

THIS book contains what the author describes as the fundamentals of electricity and magnetism for general degree students. It can be recommended without reservation. Throughout, it shows the mark of the experienced teacher, who knows where stress should be laid and where difficulties lie for students. He pays proper tribute to the pioneers—Faraday, Curie, and so on—so that students can see how the various branches of the subject have arisen.

The M.K.S. system is not used because the author claims that it has no academic (as distinct from utilitarian) value. This is probably true; nevertheless, it is a pity that he has also rejected the idea of differentiating between the dimensions of $B$ and $H$ and of $D$ and $E$, an offshoot of the M.K.S. approach. Thus, in discussing dimensions he has to say, for example, "if we suppress the dimensions of $\varkappa$" (p. 700) and that the equation $\mu = \mu_0 + 4\pi\chi$ is better than $\mu = 1 + 4\pi\chi$.

But this is a minor criticism in an otherwise admirable book. It is a pity that, on the grounds of expense, a chapter on electromagnetic waves could not be included; a treatment of this subject in the same vein as the rest of the book would have been invaluable.

H. LIPSON

## Valency

Classical and Modern. By Dr. W. G. Palmer. Second edition. Pp. xi+244. (Cambridge: At the University Press, 1959.) 30*s*. net.

THE first edition of this book was published in 1944. It became deservedly popular as a good down-to-earth account of valency, with a pleasant historical flavour, and closely related to observable chemical behaviour. No less than three reprints were called for. Now Dr. Palmer has brought forward a new edition. It must be said at once that this new version preserves the admirable qualities of the older one; and the author has taken the opportunity to correct a few of the slips that had crept in. But, without extending the size of the book, he has added more information about the transition elements, the ubiquitous hydrogen bond and electron-deficient compounds. This additional material enhances the value of the book.

The author is at his best when describing, and collating, experimental results, and many of his tables of numerical data will be exceedingly valuable. But he is less confident with the more theoretical side of the field. Thus a false account of the energies of the molecular orbitals in oxygen still survives, the words 'ligand-field-theory' do not appear in the index, nor (I believe) in the text, and very little explanation is offered for the hydrogen bond. But these are minor blemishes in a useful and sensible account.

C. A. COULSON

# TUNGSTEN-185 FROM NUCLEAR BOMB TESTS AS A TRACER FOR STRATOSPHERIC METEOROLOGY

By Dr. HERBERT W. FEELY and Prof. JEROME SPAR*

Isotopes, Inc., Westwood, New Jersey

THE introduction of artificial radionuclides into the atmosphere by nuclear bomb tests has provided meteorologists with new tracers for the study of atmospheric circulation and mixing processes. In particular, the high-yield weapons that were detonated between 1952 and 1958, and which injected large quantities of radioactive dust into the stratosphere, have presented atmospheric science with several useful tracers for the study of stratospheric meteorology.

To account for the low water vapour content of the stratosphere, Brewer[1] had suggested the existence of an organized meridional circulation with air moving upward through the equatorial tropopause, then horizontally poleward at high levels, and sinking back into the troposphere in the polar regions. A similar circulation was later accepted by Dobson[2] to explain the ozone distribution in the atmosphere. Dobson, to account for the seasonal variation of ozone, suggested that cold air from high altitudes over the winter pole sinks to lower levels in the late winter or early spring, bringing high ozone concentrations with it. The 'Brewer–Dobson' circulation model was adopted by Stewart *et al.*[3] as a reasonable explanation of the observed variations of radioactive fall-out with latitude and time. Machta[4] and others[5–8] have also found the predictions of the 'Brewer–Dobson' theory compatible with measurements of fall-out at ground-level. Hagemann *et al.*[9] used the 'Brewer–Dobson' model to explain the observed stratospheric concentrations of carbon-14 from bomb tests, and Burton and Stewart[10] employed it in their explanation of the stratospheric concentrations of the radon daughter products.

An alternative theory of the effective transfer processes in the stratosphere was proposed by Spar[11], who suggested that large-scale horizontal mixing (turbulent diffusion, 'Austausch') plays a dominant part in the dispersion of radioactive debris in the stratosphere. In the lateral mixing theory the 'gap' between the tropical and polar tropopauses is considered to play a significant part in the transfer, by horizontal motion, of debris from the stratosphere to the troposphere.

Data recently obtained by the High Altitude Sampling Program on the dispersion in the stratosphere of debris from the United States 'Hardtack' nuclear weapons tests of 1958 appears to be in contradiction to the 'Brewer–Dobson' model, but are apparently consistent with the hypothesis of lateral mixing as the most effective exchange agency. The data on which this conclusion is based are the measurements of the unique tracer tungsten-185, which was produced in several of these equatorial shots.

The sampling programme[11–13] has involved the collection of filter samples of stratospheric air in a meridional-vertical plane in the western hemisphere extending from the North Pole to 57 degrees south. The samples are collected by Lockheed *U*-2 aircraft, and are analysed for fission products including strontium-90 as well as other artificial and natural radionuclides such as plutonium, tungsten-185, rhodium-102 and beryllium-7. The data on the distribution of tungsten-185 in the stratosphere are especially relevant to the attempts to describe stratospheric transfer processes.

About 95 Mc. of tungsten-185 were injected into the stratosphere during the 1958 'Hardtack' tests[13] near latitude 12° N. between May and July of that year. Tungsten-185 decays with a half-life of 74 days, so that it is necessary for the geophysical analysis of tungsten data to correct for the radioactive decay rate. All the tungsten data referred to here have been corrected for radioactive decay to a common date of August 15, 1958.

So far as is known, tungsten-185 was only produced in significant quantities by the few 'Hardtack' weapons. It is therefore a unique tracer, having been injected at one place only, the Bikini–Eniwetok area at about 12° N., and within a limited time-interval, unlike strontium-90 which has been injected over a period of six years at high and low latitudes. The tungsten data therefore offer an excellent opportunity to study the dispersion of a cloud of radioactive particles injected into the tropical stratosphere.

The debris from the 'Hardtack' tests spread rather quickly through the stratosphere. By late 1958 tungsten-185 was included in the stratospheric debris which was falling out in north temperate latitudes[14]. Tungsten-185 was detected in most filter samples of stratospheric dust collected by the High Altitude Sampling Program on and after May 24, 1958.

Vertical profiles of tungsten-185 and strontium-90 (expressed in disintegrations per min. per 1,000 standard cu. ft. of air: abbr. d.p.m./1,000 s.c.f.) are shown in Fig. 1 for four ten-degree latitude belts for the period November–December 1959. The distribution of tungsten-185 at this time was similar to that which had existed as early as September 1958, except for the fact that the peak concentration and the vertical and horizontal gradients have diminished. During this entire period the maximum tungsten-185 activity has been located between 10° N. and S. and close to the 70,000-ft. level. (During July–August 1959 the maximum lay clearly below 70,000 ft. in the equatorial zone.) At higher latitudes the level of maximum tungsten activity is found at lower

* Professor of meteorology, New York University.

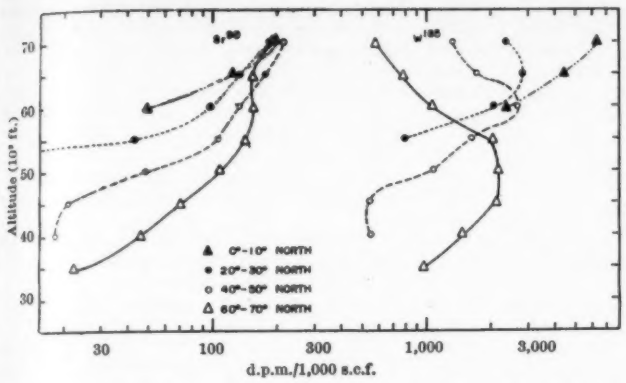


Fig 1. Vertical profiles of strontium-90 and tungsten-185 (corrected for decay to August 15, 1958) in the lower stratosphere during November–December 1959

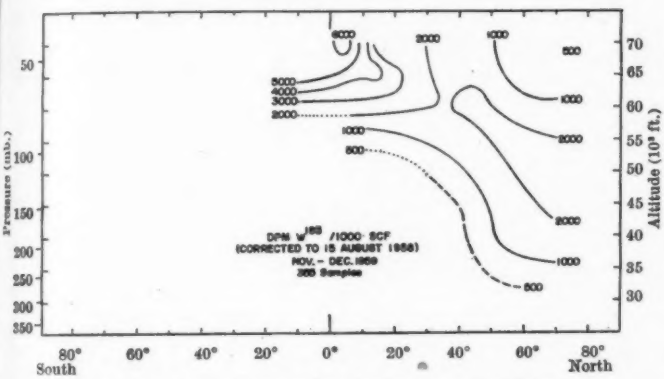


Fig. 2. Mean distribution of tungsten-185, November–December 1959

altitudes, diminishing in height toward the Pole. Data for the southern hemisphere were obtained only up to August 1959. Up to that time the distribution of tungsten-185 was roughly symmetrical about the equator, but with somewhat lower activity in the southern hemisphere. This pattern differs from that of the strontium-90 shown in Fig. 1, which, at all latitudes, shows maximum activity at the maximum sampling altitude of the aircraft.

The tungsten-185 distribution is shown more clearly in the meridional-vertical cross-section for November–December 1959 (Fig. 2). Here can be seen the virtually stationary 'core' of the tungsten cloud over the equator, and the layer of maximum tungsten activity sloping downward toward the North Pole. The slope of this zone of maximum tungsten, it may be noted, does not parallel the isentropic (potential temperature) surfaces in this region of the atmosphere, for the latter are nearly horizontal. Fig. 3 is a schematic cross-section showing the relation between the layer of maximum tungsten-185 and the tropopause structure.

According to the 'Brewer–Dobson' model, tungsten-185 should have reached the lower polar stratosphere by moving upward into the high tropical stratosphere, migrating poleward at high altitudes, and then descending into the lower polar stratosphere. However, since 1958, and at least until April 1960, the highest tungsten concentrations have been found in the equatorial stratosphere at 65,000–70,000 ft., indicating no significant upward motion of the debris in that region. Furthermore, high concentrations of tungsten have never been found at the 65,000–70,000-ft. sampling altitudes in the polar stratosphere, indicating that the movement of this nuclide into the lower polar stratosphere, where the higher concentrations are found in these latitudes, has not been due to subsidence of air and debris from the high polar stratosphere.

The observed distributions of tungsten-185 suggest a lateral spreading by turbulent 'Austausch' from the latitude of injection, at about 12° N., into both the northern and southern polar stratosphere, as indicated by the arrows in Fig. 3. The lateral mixing appears to have occurred within a sloping layer which decreases in height toward the poles. The fact that the 'mixing surface' slopes more steeply than the isentropic surfaces may indicate the existence of a systematic sinking of the radioactive debris relative to the air as it mixes poleward, possibly by gravitational settling or some other mechanism, or a systematic subsidence of the air itself as it mixes into the polar regions. There is no indication, however, of a large-scale subsidence of polar stratospheric air from very high levels.

The profiles of strontium-90 shown in Fig. 1 are consistent with the concept of lateral mixing, if there exists a zone of maximum strontium-90 con-

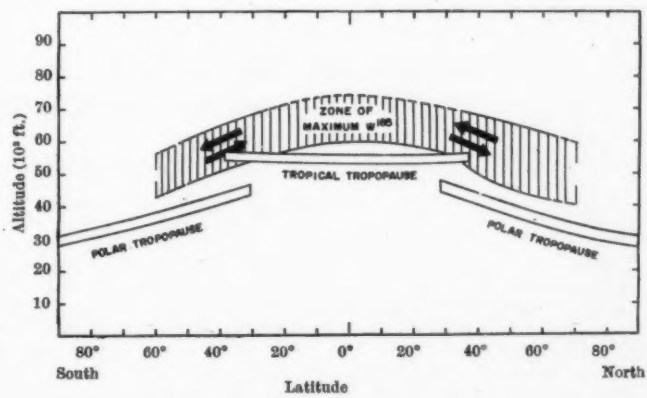


Fig. 3. Zone of maximum tungsten-185 concentration

centration which is broader and at a higher altitude than the zone of maximum tungsten-185 but roughly parallel to it. Such a distribution of strontium-90 was probably produced by the high-yield 'Hardtack' weapons in the summer of 1958. The high concentrations of strontium-90 found at high altitudes in the polar stratosphere may then be explained as the result of lateral spreading of this debris. Prior to the 'Hardtack' tests, our data indicated a distribution of strontium-90 similar to the present distribution of tungsten-185. Of course, the strontium-90 data are not as easily interpreted as the tungsten-185 data due to the presence of some strontium-90 from Soviet high-latitude tests.

The distribution of ozone in the stratosphere, which was accounted for by the 'Brewer–Dobson' model, may also be interpreted in terms of the mixing model presented here. Ozone is produced in high concentrations in the tropical stratosphere below 100,000 ft., the same region that received injections of strontium-90 from high-yield 'Hardtack' tests. According to Paetzold[15], the relatively high ozone concentration found below 65,000 ft. in the polar stratosphere and the deficit of ozone found below 89,000 ft. in the tropical stratosphere, as well as the seasonal variations in ozone, suggest the existence of a meridional transport of ozone toward the poles in the layer from 50,000 to 80,000 ft. Such a transport may certainly be effected by lateral 'Austausch'.

The increase in the rate of fall-out of nuclear debris in the north temperate zone, which has been observed during the early spring of each year, is attributable, in part, to a rise in the concentration of nuclear debris in the lower polar stratosphere during the winter as a result of the influx of debris from lower latitudes. This influx occurs in response to increased rates of turbulent mixing within the winter stratosphere. During the late winter and early spring this material is released to the troposphere by turbulent mixing through the tropopause and through the tropopause gap, and by the raising of the tropopause with the onset of warmer weather. The early spring increases in fall-out rate in 1956, 1957, 1958 and 1959 were augmented, as Martell[16] has suggested, by debris injected into the polar stratosphere during the latter half of the preceding year. As Walton[14] has pointed out, however, fall-out in the north temperate latitudes during the first six months of 1959 appeared to come from a well-mixed source, presumably an area of the lower polar stratosphere, which contained debris injected into the lower tropical stratosphere by United States tests in the summer of 1958 as well as debris injected into the lower polar stratosphere by Soviet tests during the autumn of 1958. Such a stratospheric source could have resulted only from extensive turbulent mixing between bodies of polar and tropical air during the winter of 1958–59.

It would appear that the data on the distribution of most natural and artificial tracers in the stratosphere (and data on the surface distribution of fall-out of stratospheric origin) can be explained as well by a stratospheric mixing and transfer model which invokes turbulent mixing as the most effective process as by one which invokes an organized meridional circulation. However, data on the distribution of tungsten-185 in the stratosphere can be interpreted much more easily in terms of the former model, although the exact configuration of the apparent mixing surfaces has not yet been adequately explained.

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# ORIGIN OF THE PACIFIC BASIN: A METEORITE IMPACT HYPOTHESIS

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VERY little is known about the processes that have fashioned the major features of the Earth's surface. Of the many problems unsolved, perhaps one of the most intriguing of all is that of the origin of the Pacific Basin.

It is known that the lighter crustal layers, which form the continental land masses to a depth of 20–40 km., are relatively thin on the ocean floors and in the particular case of the Pacific Basin are almost entirely absent[1–3]. The Pacific Ocean itself has a mean depth of 5 km. and occupies almost half the Earth's surface; the greater density of its underlying rocks is consistent with the absence in the gravitational potential of any first harmonic terms about the axis of rotation[3]. It was pointed out by Suess in 1888 that an outstanding characteristic of the Pacific

is that it is surrounded by a variety of features which lie parallel to its coastlines. Among these features are the island festoons and the multiple arcs of deep-focus earthquakes, gravity anomalies, and ocean deeps. A further impressive characteristic is the seismic passivity of the Pacific Basin itself, which is in direct contrast with the continual tectonic activity in the surrounding regions where dissimilar crustal structures are in close contact and the land masses are folded as if by thrust against the denser and stronger mass of the Pacific Basin.

To explain such major surface characteristics it is proposed that the Pacific Basin was the seat of an immense explosion in the primitive Earth, and that the explosion was possibly due to a collision with a planetesimal or a satellite of approximately 100 km. radius. An attempt will be made to show that the explosion excavated a large crater of several thousand kilometres in radius and some hundreds of kilometres in depth. The great masses of material that were swept back and dropped at the rim of the crater formed the discontinuities of crustal structure and composition which survive to the present day and are responsible for the peripheral features of the Pacific Basin. Following the recovery of hydrostatic equilibrium there remained a shallow and permanent crater depression (because of the absence of the lighter surface layers) which is the present Pacific Basin.

There are very few theories which attempt to account for the absence of the lighter crustal rocks on the ocean floors and in the Pacific Basin. A well-known theory is that due to Fisher, who, in 1889, elaborated on the idea that the Moon originated from the Earth with the suggestion that the Pacific is the scar left by this event. The idea that the Moon originated from the Earth was further developed by G. H. Darwin with the tidal resonance hypothesis. However, detailed analyses, particularly by Jeffreys, have cast doubt on the whole idea that the Moon originally was in some way wrenched from the Earth. A particularly strong argument against such ideas is that, failing the coincidence of a third body in the immediate neighbourhood, the ejected Moon would most likely fall back and in any event could not become a satellite of the Earth.

In an alternative theory, Hills[4] has more recently proposed that the lighter crustal rocks such as granite were concentrated into continental rafts by the convection currents that occurred while the Earth was solidifying from a molten state. A comparison is made with boiling jam in which the convection currents sweep the scum on the surface from the centre to the sides. There are a number of difficulties with any theory of this kind, among which are Urey's[5] arguments in favour of formation of the Earth while in a relatively cold state. However, if the Earth was at some time in a molten state the present surface rocks, which are likened to the scum formed on jam, were not necessarily the first materials to solidify, but in all probability were the last. Most materials have a greater density in the solid than in the liquid phase; also, the melting points of silicates increase considerably with depth; hence it is highly unlikely that a solid crust of substantial thickness would first form and then float on a liquid or even a semi-liquid mantle. It would seem that the major event which led to the destruction of the surface symmetry happened while the Earth was in a solid state.

In any discussion of this kind the Moon's surface is of prime interest. The processes which formed the lunar surface may also have been active on the terrestrial surface in the past. But unlike the Earth's surface the salient features of the Moon have not been effaced by erosion. There is little doubt that the majority of the large craters on the Moon were formed by explosions and it is now agreed by most[5-8] (who have argued quantitatively in this field) that the most plausible explanation is that the craters were produced by the explosive impact of incident bodies of various sizes, compositions, and relative velocities, falling singly or in groups. Covering large areas of the Moon are the maria, which may be either lava floods or compacted fragmentary material presenting a similar appearance[9,10]. The processes which produced the craters and the maria appear to have operated simultaneously; the numerous craters continually erupted and tended to obliterate the maria, and the maria less-frequently swept out and covered the existing craters. There is no reason for believing that there were not several cycles or even a continuous history of mutual obliteration in which at any instant, including the terminal period of the process, the Moon had in principle the same kind of surface features as it has now.

In 1893, Gilbert[11] argued strongly against a volcanic origin of the maria and was the first to point out that the evidence is consistent with the idea that the maria were also formed by collisions. He directed attention to the fact that Mare Imbrium, the largest of the maria, with a diameter of about 1,000 km., was surrounded by belts of mountains and radially directed furrows and splashed surfaces as if a great explosion had blasted material in all directions. Baldwin has given considerable support to this view and states that ploughed and splashed surfaces can be detected radiating from some of the other maria. Urey and Kuiper have developed the idea further, and the former ascribes the origin of Mare Imbrium to the oblique impact of a large meteorite of 100 km. radius.

Whether or not the explosive upheavals which formed the maria were plutonic or meteoritic in origin, the main suggestion is that the Pacific Basin was formed by a similar but even larger explosion. No known plutonic mechanisms appear to be adequate, and we shall therefore leave aside the question of a plutonic origin and proceed with the assumption that the Pacific Basin was formed by an explosive impact.

The multiple objects that were incident on the Earth and Moon some $10^9$ years ago or more were not improbably the remnants of the birth processes peculiar to the Earth–Moon system. Either the objects were satellites of this system, or they were planetesimals which were swept up in some tens of millions of years[12]; or possibly a combination of both. In the first case the energy $\varepsilon E$ released per unit mass of a satellite on impact with the Earth is given by $\frac{1}{2} \leqslant \varepsilon < 1$, where $E$ is the escape energy of $6 \times 10^{11}$ ergs gm.$^{-1}$ from the Earth; in the second case, the energy released per unit mass of a planetesimal in most cases is given by $\varepsilon > 1$ and depends on the form of the orbit. If the object had a mean density of 3, roughly equal to that of the Moon, the total energy released by the collision was $10^{24}\alpha^3\varepsilon$ ergs, where $\alpha$ is the radius of the satellite (or planetesimal) measured in units of 100 km.

The physics of crater formation by explosive impact are complex, and are still in an initial state of development. In the case of large craters the following rather crude arguments give results which are possibly sufficiently accurate for the present purpose. It happens that for $\varepsilon > \frac{1}{4}$ the meteorite has a relative velocity $v$ which in many instances is greater than the propagation velocity of longitudinal waves in the Earth's outer layers, and a one-dimensional fluid treatment is adequate for the first stages of the impact. (This is not necessarily true for the Moon, and it seems likely that the maria are not true explosion craters, but are mainly compacted and sintered beds of the fragmented impacting body.) During the collision, shock fronts advance into the Earth and the meteorite, and behind the shock fronts a compacted region of high pressure and temperature builds up and moves into the Earth with a velocity of $\frac{1}{4}v$ (assuming that the meteorite and the outer layers of the Earth have the same density). When the shock front reaches the rear end of the meteorite, rarefaction waves develop and the explosion commences. From the conservation of momentum and energy one finds that at the instant the explosion commences the compacted region has a total mass twice that of the original meteorite, and a kinetic energy half that of the original meteorite; the remaining half of the kinetic energy has been converted into heat and other forms of internal energy in the compacted region. Following this instant, the one-dimensional model progressively breaks down as the compacted mass bores down into the Earth. However, we have that at least half the original kinetic energy of the meteorite is available for the explosion and is converted entirely into heat as the compacted region expands into a gas (the ionization energy of the intermediate plasma state is also eventually available as heat), and at the most only half the original kinetic energy is propagated into the Earth and uphurls large areas of the surface and sets the Earth into large-amplitude oscillations.

Gilvarry and Hill[13] have calculated the temperature and pressure in the compacted region using an equation of state based on the statistical Thomas-Fermi model of the atom. However, it is essential to remember that the moment expansion commences their results no longer apply, and one finds that the temperature tends towards that of an ideal gas of 24,000 $\varepsilon$ °K. for an average atomic weight of 20. From Gilvarry and Hill's calculations it is found that for $\varepsilon \simeq 1$ the density in the compacted region prior to the explosion has been increased by 8/5, and therefore the shock fronts have velocities of $4v/3$ (downwards) and $-v/3$ (upwards), and the meteorite plunges into the Earth a distance equal to 3/4 of its diameter before the explosion begins; or for $\varepsilon \simeq 3$, the density is increased by 2, the shock velocities are $v$, 0, and the meteorite penetrates a distance of 1 diameter.

The complexity of the phenomena involved makes it extremely difficult to estimate the dimensions of the crater formed by an explosion. In general, the crater is large in comparison with the size of an exploding missile. The extrapolation of known data on crater dimensions by the empirical scaling rules used in nuclear explosions[14] means that for very large craters the energy released approaches, and can even be less than, the necessary work done against the gravitational field. If $W$ is the energy released, it is usual to assume that the crater radius varies as $W^{1/3}$ and the depth as $W^{1/4}$. It follows that the work done against the gravitational field is proportional to volume × depth, or $W^{7/6}$. Since the work done must be less than $W$ there is a limit beyond which these scaling rules cannot be applied. This limit occurs for very large craters where the gravitational field plays the dominant part in determining their size. Baldwin's empirical formulæ, which are quadratic in logarithms and therefore yield indices which are functions of the crater size, also encounter, so it appears, a similar difficulty, particularly when it is remembered that the final depth of a large crater may be very much less than its initial depth. It is also important to remember that in the case of very large craters the final depth (which is the parameter used in the scaling rules and the empirical relations), after the recovery of hydrostatic equilibrium, cannot depend solely on $W$ but must also depend on the density gradient at the surface of the Earth; if there is no density gradient the final depth is zero and is independent of the value of $W$.

It would seem plausible, therefore, to assume that for an explosion of the magnitude and nature that we are discussing the initial crater dimensions are determined primarily by work done against the gravitational field. Thus, if all the kinetic energy $(4/3)\pi a_s^3 \rho_s \varepsilon E$ of the meteorite is expended in excavating a crater of radius $R$, the minimum work done against the gravitational field for a conically shaped crater (that is, the depth relative to the Earth's curved surface changes linearly) of maximum depth $d$ is $\pi R^2 d^2 \rho_e g/12$. If we now suppose that the maximum depth is approximately the radius of the satellite, or $d \simeq a_s$, then it follows that:

$$R^2 \simeq 16\varepsilon a_s a_e \rho_s \rho_e^{-1} \qquad (1)$$

since $E = g a_e$. This estimate represents an upper limit to which crater radii tend for very large explosions. It neglects the effect of the curvature of the Earth's surface, and also the possibility that material escapes from the Earth. We have seen that the internal energy density of the compacted region is $\frac{1}{4}\varepsilon E$, and for $\varepsilon > 2$ there is the possibility that a fraction of the ejected material encircles the Earth and is deposited as rays similar to those observed radiating, for example, from Tycho; also for $\varepsilon > 4$ it is not unlikely that some of the ejectamenta escape from the Earth. In any event, the existing proto-atmosphere would be blown away either completely or partly from the Earth; this would expend only a negligible amount of the available energy if the total mass of the proto-atmosphere was of the same order of magnitude as the mass of the present atmosphere. From the abnormally low abundances of the inert gases it is known[15] that at some stage the Earth must have lost its original atmospheric envelope, and that the present atmosphere is of secondary origin and was formed by chemical and photosynthetic processes acting on juvenile gases from the Earth.

Assuming that $\varepsilon \simeq 1$, and $\rho_s \simeq \rho_e$ for the surface layers of the Earth, we find that for meteorites of radii 100 km. and 500 km. the crater radii are approximately 3,000 km. and 7,000 km., respectively. It is remarkable that Baldwin's empirical formula, which is constructed from the known data of comparatively small explosions, gives crater radii of approximately 2,500 km. and 7,000 km. A crater of radius 3,000 km. is possibly adequate to account for the size of the Pacific Basin. The hypothesis therefore is

that a satellite or planetesimal with a radius of approximately 100 km., and $\varepsilon \simeq 1$, penetrated a distance of 100–200 km. and exploded; the expanding gases released an energy of the order of $10^{24}$ ergs and swept back the surface layers to form a crater, at the edge of which large quantities of material were dropped; almost simultaneously there was hydrodynamic flow in the Earth caused by the subsiding rim and the rising crater floor, and the gravitational energy released caused considerable melting over a wide area; finally, there remained only a relatively shallow depression surrounded by a slightly elevated 'land mass' of lower density and dissimilar composition.

Perhaps it should be emphasized that an explosion of this magnitude bears no comparison with any known terrestrial event. In terms of present-day nuclear weapons the total energy released was of the order of $10^{11}$ five-megaton hydrogen bombs, and over an area of 3,000 km. radius this amounted to a mean energy density of approximately 1 atom-bomb (20 kiloton) per square metre. Using Einstein's mass-energy relation, it is found that the total energy released is equivalent to a loss of mass of $10^{13}$ gm., or a mass weighing approximately $10^7$ tons.

Of all the assumptions that one might make the simplest is that the collision was made by a planetesimal, such as one of the large asteroids. In the past there may have been many such bodies with orbits close to that of the Earth. This point of view raises the possibility that there may have been multiple encounters with the Earth of the particular kind that we have considered with $\varepsilon > 1$. It is then logical that one should go even further than has been implied so far in this discussion, and ask: Is it conceivable that all the ocean basins, underlaid by rocks denser than the surrounding land masses, are crater depressions produced by explosive impacts and have in common the same origin as the maria on the Moon?

As an alternative approach it is not improbable that the Earth once possessed more than one natural satellite, and that the particular collision we have considered was made by a satellite that was deflected from its normal orbit by a third body such as the Moon, or was sufficiently close to lose angular momentum by tidal friction. In the case of several satellites a close examination of the mechanics involved is necessary to establish whether the idea of multiple collisions with the Earth is at all valid. The possibility that the early Earth possessed two 'moons', which moved apparently in opposite directions across the sky in very much the same way as Phobos and Deimos appear to move from Mars, is sufficiently intriguing, however, to consider briefly some conditions for a collision caused by tidal friction.

Quite what the conditions were like for tidal friction is not known; but according to Jeffreys's calculations the Moon was at approximately 0·6 of its present distance some $4 \times 10^9$ years ago. For a satellite to spiral inwards it must be close enough to rotate faster than the Earth's surface, or since the day was then only 7 hr. long, this requires that the satellite's distance $r_s$ satisfied $r_s < 3a_e$. If the conditions for tidal friction were the same then as now, the time taken by a satellite of 100 km. radius to reach the Earth would not exceed $10^6$ years and would be considerably less in the event of tidal resonance. But also any satellite at the present moment at a distance of approximately $r_s < 7a_e$ spirals inwards because of tidal friction. It follows that if initially the satellite was at a distance $3a_e < r_s < 7a_e$, and if the tides raised by the Moon were larger than those raised by the satellite, then the satellite would first have spiralled outwards and when the Earth's surface rotated faster would then have spiralled inwards. The condition that the Moon raised the larger tides is that $a_s/r_s < a_m/r_m$, or the sufficient condition is that the satellite had a radius of less than 130 km. At distances less than the Roche limit of 2–3 Earth radii a fluid satellite has no equilibrium configuration, and therefore it breaks up. But in the case of a solid satellite one finds that the maximum differential force due to the Earth's gravitational field is less than the internal strength (assuming a critical stress difference of $10^9$ dynes cm.$^{-2}$) for radii of less than 120 km.; therefore a solid satellite with a radius smaller than 120 km. does not break up. A more detailed analysis by Jeffreys[16] gives substantially the same result. It seems therefore that a satellite of approximately 100 km. radius at an initial distance of less than approximately 7 Earth radii would at some time in the past have struck the Earth, would also have remained a coherent body without fracture as it approached the Earth, and in the final collision could have released perhaps just sufficient energy to account for the Pacific Basin. It must be emphasized that this rudimentary picture is totally inadequate if one adopts the point of view that there has been more than one large collision with the Earth. As we have seen, a single such collision is sufficient to affect profoundly the fluid envelopes in which the tidal friction occurs; without a closer examination of the problem one might say that this reason alone weakens the idea that several collisions were due to tidal friction.

Baldwin has made the suggestion that there should be geological evidence in the pre-Cambrian rock strata of repeated meteoritic impacts with the Earth. In this discussion I have taken the suggestion one stage further. On making the reasonable assumption that at least one body has collided with the Earth comparable in size with that responsible for producing Mare Imbrium, it follows that the evidence for such a collision should be immediately apparent even nowadays if it is looked for on a sufficiently large scale. It is proposed that the Pacific Basin has many characteristics that strongly suggest an origin of this nature.


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# EXPERIMENTS WITH DIVING SEALS*

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ALL mammals can withstand complete submersion in water for a little while; but some forms are able to remain submerged at considerable depths for remarkable periods of time. It will be obvious that there are few accurate observations on the maximum length of time for which any mammal can remain under water: it would mean diving the animal to extinction. The following is a list of record durations of dives that have been taken from Scholander[1], Scheffer[2] and Harrison and Tomlinson[3]:

| | | | |
|---|---|---|---|
| Pigeon | 1 min. | Ringed seal | 20 min. |
| Hen | 3 min. | Common seal | 28 min. |
| Duck | 17 min. | Porpoise | 12 min. |
| Penguin | 7 min. | Blue whale | 50 min. |
| Water rat | 2 min. 17 sec. | Sperm whale | 75 min. |
| Rabbit | 3 min. | Bottle-nosed whale | 120 min. |
| Dog | 4 min. 25 sec. | Man (pearl and sponge divers) | 2 min. 30 sec. |
| Muskrat | 12 min. | | |
| Grey seal | 20 min. | | |

The maximum depth reached by a diving animal is as difficult to determine as the duration of a dive. The literature is full of anecdotes of fouling of cables, hooks and nets by seals and whales at immense depths; but there is no evidence that the animals were not dying before they became entangled or whether they would have survived had they returned to the surface. The following are a few recorded deep dives (see references for duration):

| | | |
|---|---|---|
| Penguin | at least 12 m. | Experimental dives |
| Weddell seal | 92 m. | Diving below ice |
| Common seal | 92 m. | Experimental dives |
| Grey seal | 146 m. | Caught on hook |
| Harp seal | 273 m. | Caught on hook |
| Porpoise | 20 m. | Line attached |
| Fin whale | 355 m. | Line attached |
| Sperm whale | 900 m. | Entangled in cable |
| Man | 165 m. | Flexible suit with special breathing mixture |

All evidence indicates that young seals and whales cannot equal the performance of adults. Scholander[1] records that a 4-month-old grey seal pup on its first swim in deep water dived to 22 m. for a total time of 1 min. A 6-month-old hooded seal dived spontaneously to 75 m. and remained submerged for more than 4 min. A young hooded seal, which had been submerged the previous day for 18 min., was weighted by Scholander and submerged to a depth of more than 300 m. in 3 min. It was drawn to the surface immediately after reaching that depth over a period of 9 min. The seal was reflexless on return to the surface, its heart beat very weakly, one pupil was widely dilated, one a short slit, the nostrils were firmly closed and it died shortly afterwards. No water was found in the lungs, but there was an abundance of air bubbles in the mesenteric arteries. Death was presumed to be due to air embolism.

Our experiments were carried out on pups, yearlings and adolescent common seals (*Phoca vitulina*) obtained from the Wash, East Anglia, through the kind co-operation of the Eastern Sea Fisheries Joint Committee and the Hydrographic Survey Ship, H.M.S. *Scott* (Commander H. R. Hatfield, R.N., then in command). Diving performance was assessed by immersion in a shallow tank, at sea, and under water or in air in a pressure-chamber capable of simulating a pressure of 300 ft. of water. Seals were secured to a board in a fashion similar to that described by Scholander[1], or in a specially designed lace-up 'Terylene' harness to enable free-swimming to take place at the end of ropes. Leads were connected from axillary electrodes to a portable Elmquist electrocardiogram. When required, animals were anæsthetized with 3–10 ml. of a solution of 1 gm. in 40 ml. sodium thiopentone injected into the extradural vertebral vein as if performing a lumbar puncture. Anæsthesia was afterwards maintained by introducing a Magill endotracheal tube (child's size) and administering nitrous oxide and oxygen.

Investigations of heart- and respiratory-rate were made on pups and young seals out of water, and the heart-rate was recorded during all experimental dives. The animals were secured as loosely as possible to a board or harness and were not anæsthetized during the dives unless specifically stated. No animal was 'dived' again unless the heart-rate and behaviour had returned to conditions prevailing at the beginning of the first dive.

## Heart-rate Surfaced

This displays considerable variation, and even irregularity, in all animals whatever their age and whether or not they have recently dived. Young pups have a resting heart-rate of 90–180 beats per min.; in 2–3-year-old adolescents it varies from 75 to 180 beats per min. Proximity to the investigator or indication to the seal that it is about to dive (by submerging it a number of times for a few seconds) does not unduly influence the heart-rate. Any tachycardia that resulted from a struggle to secure the seal to a board, or in its harness, soon subsided and seals often went peacefully to sleep during a pause in a diving programme.

Respiratory-rate out of water is comparatively regular at 18–20 per minute, in both pups and adults. It is less regular when the seal is immersed in a harness with only its nostrils above water. The heart-rate increased from 112 to 144 when a seal was immersed suddenly up to its neck, head still above water, and fell to 120 after 5 min. It occasionally slowed from 120 to 60 for a few seconds following a respiratory pause longer than normal. This slowing of the heart associated with changes in respiratory-rate has been described also by Irving, Solandt, Solandt and Fisher[4] and Irving[5]. Forcible closure of the nostrils and mouth of a seal out of water (so as to prevent respiration) caused a fall in heart-rate from 130 to 80 after 5 sec., to 48 after 22 sec., to 15 after 68 sec., and was followed by violent struggling which prevented further recordings. One yearling common seal was anæsthetized (with thiopentone, intubated, and then nitrous oxide and oxygen mixture used to continue the anæsthesia) and an attempt was made to determine the effect variations in respiratory-rate

* Substance of a Friday Evening Discourse delivered to the Royal Institution on November 11.

would have on heart-rate. Increasing the respiratory-rate artificially to 40 for a period of 2 min. had no appreciable effect on the heart-rate. The respiratory-rate was then lowered to 5; after 1¼ min., when the heart-rate had dropped to 17, the animal collapsed, but was later resuscitated.

Tweaking the vibrissæ caused episodic slowing of the heart-rate to 75 beats per minute for a few seconds; smacking the face raised the rate to 165 beats per minute. Throwing cold water over the face had little effect on the heart-rate.

## Shallow Dives

Animals were 'dived', secured on a board, for periods of up to 28 min. In a dive of this length, intermittent struggling started at 15 min. and became extreme during the last minute so the animals were brought to the surface. The diving bradycardia did not develop as rapidly as in *Halichoerus*[1]; the slowest heart-rate (6 beats per minute) occurred between 1 and 3 min. after diving. Thereafter the heart-rate gradually increased as time passed. The degree of bradycardia and the rate at which it developed were not significantly affected by the rate at which the heart was beating before the dive commenced. Repeated diving of the same animal (after a short recovery period of a few minutes) did not influence the rate of onset, degree of bradycardia or recovery behaviour. There was always a recovery tachycardia lasting for 5–10 min. after a dive of more than a few minutes. The slowest and longest lasting bradycardia was observed in older seals: the bradycardia also developed more rapidly.

A two-year-old seal was secured in a harness that left its head, four flippers and tail free; guide ropes and electrocardiograph leads were attached. The animal swam freely in a shallow tank, and dived for periods of several minutes. The heart-rate showed changes similar to those recorded when the seal was secured to a board. It was noticed that the seal exhaled when it broke the surface after a short shallow dive; this observation has been frequently confirmed by us and is also mentioned by Harrison Matthews[2]. Another young seal behaved similarly in a harness when allowed to swim in the sea. It towed a small dinghy containing two men with ease at about walking speed, and afterwards towed a skin-diver for a short distance under water.

A seal secured to a board was prepared for diving in a shallow tank; before diving and throughout the dive it was forcibly prevented from opening its nostrils or mouth. The heart-rate was 144 beats per minute on the surface (nose and mouth closed) and fell to 24 beats per minute after 30 sec. It remained at that rate for 75 sec., after which it struggled so violently to exhale that no further recording was possible.

## Deep Dives

Three types of experimental diving were carried out: (*a*) pups a week old were lowered into the sea on a board; (*b*) two-year-old seals were placed in a tank filled with water inside a pressure chamber and the air pressure increased by stages to depths equivalent to up to 80 ft.; (*c*) two-year-old seals similarly secured were taken rapidly to 300 ft. and kept there for periods up to 5 min.

The pups showed an immediate bradycardia to between 10 and 16 beats per minute, but within a few minutes under water the rate began to rise to 30 beats per minute. The older animals displayed an immediate bradycardia to 4–15 beats per minute, which was maintained for 2·0–5·0 min. at depths in the pressure chamber equivalent to up to 200 ft. There was no indication in the older animals of a gradual decrease in the bradycardia as the dive progressed at a constant depth. There was, however, an increase in heart-rate as the animal returned to shallower depths. The pups often showed a marked decrease in bradycardia after quite a short period (1–3 min.) at only 20 ft. There was no noticeable change in the bradycardia of adolescent seals in dives of short duration even at 200 ft. One young seal, taken to about 100 ft., managed to raise its nostrils above the water in the pressure tank on return when at 50 ft. It appeared healthy immediately after the dive, and carried out shallow diving during the ensuing weeks without ill-effect. Three months later the seal became anorexic, lost weight and was killed. Extensive surgical emphysema was seen in the lungs, thoracic wall and vertebral venous system at post-mortem examination. It was concluded that the animal had inhaled air under pressure and ruptured a lung during the return to the surface.

A two-year-old seal was taken rapidly to a depth of 300 ft. in 4 min. 30 sec. It remained at this depth for 1 min. 20 sec. and returned to the surface by stages, pausing for 30 sec. at every 50 ft. to make electrocardiograph recordings. On return to the surface the respiratory-rate was 30 per min.; the animal appeared fit and active, and displayed no signs of 'bends'. The same animal was 'dived' to 300 ft. the next day and kept there for 5 min. Towards the end of this period the cardiac complex on the electrocardiographic recordings indicated some degree of physiological 'defeat'. The animal was returned to the surface, and its heart was beating slowly on removal from water. Its pupils were dilated, muscular movements were weak. The heart stopped a few seconds later, and the animal could not be resuscitated. At post-mortem no evidence of air embolism, lung damage or hæmorrhage could be detected. It is possible that the animal suffered a 'squeeze' at this depth such that the heart could not contract fully and cerebral anoxia followed.

Every seal was observed to exhale air when or just after it was immersed in water, and again later as the pressure increased in the chamber.

## Exposure to Increased Air Pressure

It was considered to be of interest to investigate the effect on a seal of simply exposing it to a steady increase of air pressure simulating depths equivalent to those it had 'dived' when under water. Two-year-old seals were placed in a pressure chamber and allowed to breath naturally as the air pressure was increased. The respiratory-rate was assessed by counting the nostril openings over periods of half a minute. Increased air pressure equivalent to a depth below water of 200 ft. caused a bradycardia from 120 to 30. It was not sustained, however, and the heart-rate rose to 150 for periods lasting up to 5 sec. The increase in air pressure caused the respiratory-rate to slow from 24 to 8, and it was noticed that this was correlated with the periods of most marked bradycardia. Increase in air pressure to depths equivalent to 30–80 ft. caused little slowing of the heart-rate and no disturbance of respiration. The seals were in no way embarrassed by exposure to

increased air pressure, but did seem puzzled at the strange sensation. It appeared that only when the seal held its breath was there any heart slowing, again indicating that the bradycardia is linked with interruption of regular respiration.

### Stimulation and Section of the Phrenic Nerve

A thick, striated muscle sphincter is present on the posterior vena cava immediately cranial to the diaphragm in all seals we have examined. It is supplied by branches of the right phrenic nerve[6]. To ascertain the effect of closure of the sphincter the posterior vena cava was clamped just caudal to the liver in an anæsthetized pup: this procedure had no effect on the heart-rate in a surfaced animal. The right phrenic nerve was cut in the neck under anæsthesia in several young seals and they were afterwards allowed to recover. The animals were 'dived' a few days later. In all there was an eventual bradycardia similar to that in normal animals, but the onset of the bradycardia was delayed. Stimulation for short periods of one or both phrenic nerves had no effect on the heart-rate in surfaced anæsthetized animals.

### Stimulation and Section of the Vagus Nerve

Stimulation of the intact right vagus of an anæsthetized pup resulted in slowing of the heart-rate from 120 to 22, with immediate recovery to 120 on cessation of stimulation. Stimulation of the intact left vagus resulted in disappearance of the ventricular complex on the recording: *P* waves continued to occur at 120 a minute. Stimulation of either vagus in an anæsthetized adult seal completely abolished the heart-beat for the period it was applied.

Section of the right vagus in the neck in anæsthetized pups caused no change in the heart-rate surfaced (180) and a fall to only 100 on diving. The beats were irregular. Section of both vagi in pups caused no change in the heart-rate surfaced: in an adult the rate increased from 60 to 90. In short dives other anæsthetized pups with bilateral vagal section showed no slowing of the heart. Another was anæsthetized and both vagi were exposed; it was then 'dived' and after the heart-rate had fallen to 24, both vagi were sectioned with the seal under water. There was an immediate rise in heart-rate to 156 which persisted for the remainder of the dive and after surfacing.

Discussion of the significance of some of these findings is given by Harrison and Tomlinson[3]; the parts played by various vascular modifications in seals is discussed by Harrison and Tomlinson[7] and Barnett *et al.*[8]. Further observations and discussion will be published shortly.


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# OBITUARIES

## Dr. Hugh Scott, F.R.S.

Dr. Hugh Scott, distinguished entomologist and biogeographer, died on November 1 at his home at Henley-on-Thames, at the age of seventy-five. He was born on September 16, 1885, the elder son of William Edward Scott and was educated privately and at Trinity College, Cambridge, where he was an exhibitioner and obtained a first in the Natural Science Tripos, Part I, in 1906. He received his Sc.D. in 1919.

At Cambridge Scott was deeply influenced by the training he received from Dr. David Sharp, whom he succeeded as curator of the Zoological Museum. In 1908 he joined the Second Percy Sladen Trust Expedition to the Indian Ocean and made an extensive collection of insects in the Seychelles. Scott afterwards organized the study of the collection by specialists, and himself undertook a considerable part of the work on the Coleoptera. Rarely, if ever, has a collection been so completely studied. With characteristic tenacity Scott saw the work through to completion and analysed the results in a summary of the faunal relationships of the Seychelles which is a model of clarity.

His experiences with the Seychelles fauna aroused an enduring interest in biogeography which influenced all his subsequent work. His special interest lay in the fauna of that area including East Africa and south-western Arabia where the Palæarctic and Ethiopian faunal elements meet and overlap. To further this work Scott made four long collecting expeditions in the area: to the central highlands of Abyssinia during 1926–27, the Aden Protectorate and Yemen during 1937–38, the Gughé Highlands in southern Abyssinia during 1948–49 and the Simien Mountains in northern Abyssinia in 1952–53. The extensive collections of insects and plants which resulted from these journeys provided information on areas, the fauna and flora of which were previously almost unknown. The expedition to south-western Arabia was, for example, the first in the area since that of Niebuhr in 1762. These expeditions were prepared and carried out with great thoroughness and attention to detail, and great credit is due to Scott for the tenacity with which he sought his objectives in the face of physical disability, chronic ill-health and the political obstacles of those troubled regions.

In 1930 he was appointed assistant keeper in the Department of Entomology, British Museum (Natural History), a position that he held until his retirement in 1948.

In addition to his work on the systematics of Coleoptera, Scott was an authority on the Nycteribiidae, the louse-like, wingless flies which parasitize bats. He was also the author of several works on the fauna associated with the giant lobelias and the tree senecios of the East African highlands, and on the peculiar and extensive fauna of the leaf axils of the Bromeliaceae. He also wrote a number of valuable works of a geographical nature and a book on the

expedition to south-western Arabia entitled "In the High Yemen" (1942). During the Second World War he was the chief author of the naval intelligence "Handbook on Western Arabia and the Red Sea".

He was elected a Fellow of the Royal Society in 1941, an Honorary Fellow of the Royal Entomological Society of London in 1954, and was an original member of the Entomological Research Committee formed by the Colonial Office in 1909, which later developed into the Imperial Bureau (now Commonwealth Institute) of Entomology.

Scott will be remembered by all who knew him as a kindly, courteous and deeply learned man. He was possessed of a deep religious conviction, a fact which influenced his life to a high degree.

In 1913 he married Beatrice Emily Streatfield (who died in 1947) and leaves a son and daughter.

E. B. BRITTON

## Dr. A. B. Edwards

AUSTIN BURTON EDWARDS was born in Melbourne in 1909 and educated at the Caulfield Grammar School. He graduated from the University of Melbourne with first-class honours in geology and was awarded the Howitt natural history scholarship in geology and the Bartlett scholarship. After the publication of the first two of the 128 contributions to geological science with which he is identified either as sole or joint author, he was awarded an 1851 Exhibition which enabled him to continue his studies in London at the Imperial College of Science and Technology, where he obtained his Ph.D. in 1934.

He won his university half-blue in football at Melbourne and his colours in athletics at the Imperial College; his athletics background was of great value to him in his geological work, much of which was performed in mountainous terrain.

On returning to Australia he joined the Mineragraphic Section of the Commonwealth Scientific and Industrial Research Organization, which maintains close relationships with the Geological Department of the University of Melbourne. Thus commenced a long association with the officer-in-charge of the Section, Dr. F. L. Stillwell, whom he succeeded in 1953. His early work with the Section produced a series of studies of Australian ores and ore deposits which was extended to the examination of mill products and mill tailings and eventually to smelter products such as mattes, speisses and slags. At the same time he sustained a keen interest in petrological problems and completed various papers begun in London, of which the more important were his studies on the tertiary volcanic rocks of Central Victoria and the differentiation of dolerites of Tasmania. In 1937 he shared with Prof. R. D. Wright the David Syme research prize of the University of Melbourne. He gained his doctorate of science in 1942.

His first independent mineragraphical task was the study of the occurrence of manganese in iron ore of Iron Knob in South Australia, later extended to the iron ores of the Middle Back Ranges. This was the first of a series of studies which culminated in the recognition and discovery of the oolitic iron ores in the Northern Territory and Constance Ranges in Queensland.

As the scope of work of the Mineragraphic Section widened, Dr. Edwards made contributions to sedimentary petrology, geochemistry, meteorites and geomorphology. The sedimentary petrology commenced with a study, jointly with G. Baker, of the Jurassic arkoses in Victoria, later extended to the Mesozoic and Tertiary sediments of the Aure Trough, Purari Valley and the Wahgi Valley in Papua. His interest in geochemistry arose in the past few years from studies of the selenium content in sulphide deposits and the distribution of cadmium, manganese and iron in Broken Hill sphalerites. His descriptions of meteorites were a natural extension of his mineragraphical work, while his interest in geomorphology absorbed him during his vacations.

Lecturing in the University of Melbourne on mining geology between 1941 and 1953, his interest was roused in Victorian coal. Subsequent papers on Wonthaggi and Victorian brown coals elevated him to a position of authority on brown coal and resulted in a request from the State Electricity Commission to act as geological consultant. He allocated his consultant's fees to the purchase of equipment for the Mineragraphic Section.

In 1946 a postgraduate course was provided by the Geological Department of the University of Melbourne for eight Indian graduates. Dr. Edwards contributed to this course a series of lectures on mineragraphy and ore textures. These lectures provided the basis for his book, "Textures of Ore Minerals", which the Australasian Institute of Mining and Metallurgy published in 1947 and which met with such world-wide success that the demand quickly exhausted the first edition. A new and enlarged edition (1954) was exhausted in 1960, and further reprinting was in progress at the time of his death.

In preparation for the Fifth Empire Mining and Metallurgical Congress in Australia in 1953, Dr. Edwards initiated a symposium on the geology of Australian ore deposits. It was organized by a committee appointed by the Australasian Institute of Mining and Metallurgy with Dr. Edwards as chairman. The result was a volume comprising 135 articles contributed by the leading geologists in the Commonwealth, which were edited by Dr. Edwards, with the gaps filled in with his own editorial contribution. He served as assistant editor of the *Proceedings* of the Institute until his departure overseas.

Ore minerals and their textures was the subject chosen by Dr. Edwards for the Clarke Memorial Lecture to the Royal Society of New South Wales in 1952. The last honour received by him was the award of the Society's Clarke Memorial Medal in 1960.

He was a member of the Council of the Australasian Institute of Mining and Metallurgy, Corresponding Fellow of the Edinburgh Geological Society, Foreign Member of the Mineralogical Society of India, and observer for 1958–61 for the Commission on Geochemistry of the International Union of Pure and Applied Chemistry.

In preparation for his overseas tour he acquired a knowledge of spoken Italian. He left with his wife on August 25 but died in Rome.

With his death Australian geological science suffers the loss of a brilliant and energetic scholar whose clear thinking and rapid grasp of a problem was a constant help and guide to all associated with him. This loss, at the height of his career, is most keenly felt, both throughout Australia and overseas.

F. L. STILLWELL

# NEWS and VIEWS

## Electrical Engineering at Edinburgh : Prof. W. E. J. Farvis

Mr. Farvis, senior lecturer in applied electricity and head of the postgraduate school of electronics and radio in the University of Edinburgh, has been appointed to the newly established chair of electrical engineering. He graduated B.Sc. from the University of Bristol in 1936, with first-class honours in electrical engineering. After junior teaching appointments at Dundee Technical College and University College, Swansea, he joined the Telecommunications Research Establishment in 1940, working first on new decimetric radar. The following year he transferred to counter-measures work for the radio defence of London, and for the remainder of the War led a group developing and using new ground and air interception devices. Immediately before the end of hostilities he was one of a team sent to Europe to investigate German radio and radar war-time research. In 1945 he returned to Swansea as lecturer, and in 1947 took the external B.Sc. degree of the University of London in physics. He was appointed lecturer at the University of Edinburgh in 1948, and afterwards senior lecturer. During his twelve years in the Engineering Department there Mr. Farvis has evolved a new electrical engineering degree curriculum, founded the postgraduate diploma course in electronics and radio (now in its eleventh year) and built up a research school on various types of gas discharge. His personal research has been in high-current arcs and fundamental problems associated with power-circuit interruption, interests which began during his student training at the switchgear works of the British Thomson-Houston Co. He took part in the official British programme for the International Geophysical Year, setting up stations in Shetland and Edinburgh for recording the absorption of galactic radio noise. This work, sponsored by the Royal Society, is still continuing in Edinburgh.

## The British Industrial Biological Research Association

In a written answer in the House of Commons on November 28, Sir David Eccles, as representing the Minister for Science, said that the British Industrial Biological Research Association was not designed to supplement the work of the Department of Scientific and Industrial Research. It had been formed by industry as a co-operative industrial research association, and its new laboratories were to be sited at Leatherhead on land adjacent to existing laboratories of the British Food Manufacturing Industries Research Association to facilitate the sharing of facilities. In answer to further questions on December 1, Sir David said that the laboratories would cost £56,000, and the main purpose of the facilities was to investigate the effect on health of substances used in food, or which may find their way into food from such things as pesticides, packaging materials or utensils. The site had the additional advantage of proximity to the Medical Research Council's Toxicological Research Unit at Carshalton. Questioned about the Minister's proposal to close the Research Station at Greyhope Road, Aberdeen, the Joint Parliamentary Secretary to the Ministry of Agriculture, Fisheries and Food, Mr. W. M. F. Vane, stated that the work proposed at Leatherhead was entirely different from that done at Aberdeen. During the past twelve months the latter had included : the installation and operation of the Mark I commercial prototype accelerated freeze-drying cabinet loaned from Chicago ; production of field-trial samples of various foods processed by the accelerated freeze-drying method, and of experimental rations for large-scale trials by the three Armed Services ; work on the quality and storage life of dehydrated foods ; research into problems of flavour in vegetable products ; investigation of enzyme activity in dehydrated raw meats with low-moisture content, and of the reasons for the deterioration of dehydrated raw meat ; investigation of the mechanism of oxidative rancidity and of the application of free-radical acceptors to the inhibition of oxidative rancidity induced by radiation. Three other projects had been undertaken with grants provided by the United States Department of Agriculture, including the investigation of new anti-oxidants, of the freezing and drying of muscle tissues, and of the significance of carotenoid breakdown in the deterioration of fruits and vegetables.

## Tax Assessment for Scientific Societies in Britain

Clause 9 of the Rating and Valuation Bill, which received its second reading in the House of Commons on November 30, gives effect to the recommendation of the Pritchard Committee that the total exemption from rates given by the Scientific Societies Act of 1843 to societies established for the purposes of science, literature or the fine arts, exclusively, should be terminated. In moving the second reading of the Bill, the Minister of Housing and Local Government, Mr. H. Brooke, after a tribute to the work of the Pritchard Committee, said that the Government proposed to follow the report in this difficult matter. The definition in the 1843 Act had proved so difficult to apply that he doubted if anyone would advocate its retention unaltered, and under Clause 8 of the Bill, practically every organization which now obtains benefit from the 1843 Act would in future qualify automatically for 50 per cent derating, and the local authority would have discretion to give up to complete exemption if it thought fit. As regards research associations, Mr. Brooke added, in reply to a question, that derating would turn entirely on whether an association could establish that it was a charity.

Mr. Brooke also said that the Pritchard Committee was clearly in some doubt about the position of the universities. While, as stated in the first schedule to the Bill, they were undoubtedly charities, they were also substantially financed by Exchequer grants, and, unlike other charities, many of them held a considerable if not a dominating position in the towns and cities in which they are established. Accordingly, it did not seem to the Government that a sufficient case existed for giving the universities a statutory 50 per cent exemption from local rates, although the Chancellor of the Exchequer was ready to give an

assurance that any additional rates falling on the universities in consequence would be taken into account in determining the amount of their recurrent Exchequer grants. He said also that this arrangement would not apply to the Oxford and Cambridge colleges, which as charitable foundations would receive the 50 per cent mandatory relief.

In the debate, Mr. C. M. Woodhouse challenged this discrimination between the universities and the Oxford and Cambridge colleges as contrary to the recommendation of the Pritchard Committee, although that Committee had explicitly recognized that these colleges stood in a different relation to the Exchequer from university institutions in general in that they received no financial aid directly from the University Grants Committee. Mr. Woodhouse doubted whether the distinction was valid or should be perpetuated, and pointing out that the finances of university and colleges were interlocked, observed that in its memorandum to the Pritchard Committee the Treasury had been disinclined to accept the obligation that Mr. Brooke now said the Exchequer would accept for the universities. He thought it perfectly reasonable that an increased burden on the universities should be met from the national Exchequer rather than from local funds, but that the same argument should apply to the colleges, and pointed out that in view of the decision in a test case brought last year to the Lands Tribunal by three of the colleges the effect of the present Bill would be to give the colleges double relief. A Government contribution, suggested by the colleges in their memorandum to the Pritchard Committee as the proper remedy, would avoid these rating anomalies, and Mr. Woodhouse urged the Minister to exercise his power of addition to the First Schedule and include at least the Oxford colleges.

In replying on behalf of the Government, the Parliamentary Secretary to the Ministry, Sir Keith Joseph, said that in representations before the Pritchard Committee the colleges had made it clear that they regarded the question of value as an entirely separate issue from that of rate relief. In general, the Government viewed the Oxford and Cambridge colleges as closer to educational establishments than grant-aided universities, but promised to study the point raised before the committee stage of the Bill. The question of scientific societies, and particularly the point raised by Lord Adrian in the House of Lords, was not mentioned in this debate.

## The Medical Research Council of Canada

THE National Research Council of Canada has established a Medical Research Council with responsibility for all activities formerly conducted by the National Research Council's Division of Medical Research. The new Council will have virtually complete autonomy in its operations and full responsibility for policy concerning the support of medical research, but will function under the general administration of the National Research Council. The Medical Research Council has been set up as an interim measure pending the Government's future consideration of appropriate legislation. The eventual establishment of a completely independent Medical Research Council was implied in a statement in the Canadian Parliament last summer by the Hon. Gordon Churchill, chairman of the Canadian Privy Council Committee on Scientific and Industrial Research.

Officers and members of the new Medical Research Council are: *Chairman*, Prof. R. F. Farquharson, professor emeritus of medicine, University of Toronto, vice-president (medical), National Research Council; *Secretary*, Prof. J. Auer, professor of anatomy and associate dean, University of Ottawa; *Members*, Prof. L. B. Jaques, professor and head of the Department of Physiology and Pharmacology, University of Saskatchewan; Prof. R. W. Reed, professor and head of the Department of Bacteriology, McGill University; Prof. C. B. Stewart, dean of the Faculty of Medicine and head of the Department of Preventive Medicine, Dalhousie University; Prof. M. Brown, professor of medicine, Queen's University; Prof. M. Darrach, professor and head of the Department of Biochemistry, University of British Columbia; Prof. R. Rossiter, professor and head of the Department of Biochemistry, University of Western Ontario; Prof. J. Doupe, professor and head of the Departments of Physiology and Medical Research, University of Manitoba; Prof. A. L. Chute, professor and head of the Department of Pædiatrics, University of Toronto; Prof. R. Gingras, assistant dean of medicine and head of the Department of Biochemistry, Laval University; Prof. W. C. MacKenzie, dean of the Faculty of Medicine and professor of surgery, University of Alberta; Prof. F. C. MacIntosh, professor and head of the Department of Physiology, McGill University; Prof. L. P. Bouthillier, professor and head of the Department of Biochemistry, University of Montreal; Prof. H. E. Taylor, professor and head of the Department of Pathology, University of British Columbia.

## Jubilee Celebrations in Berlin

THE Humboldt University of Berlin celebrated its 150th Anniversary together with the Charité Hospital, the 250th Anniversary of which ran concurrently. Symposia, conferences, discussions and exhibitions were offered to participants by the various faculties, including those of Medicine, Philosophy, Mathematics, Physics, Politics, Economics, Pedagogy, and Jurisprudence. The Institute of Anglo-American Literature organized lectures and discussions simultaneously. The proceedings took place during November 6–20 and enabled each faculty to give its guests noteworthy entertainment from the operatic, theatrical and musical riches which the city possesses. University dignitaries, ministerial houses and student bodies opened their doors in a succession of receptions and discussions which encouraged the informal interchange of ideas and ideals. The Faculties of Philosophy and Medicine took three days to discuss together their understanding of humanism and medicine, representational thinking, cybernetics and its role in medicine, the concept of illness and, finally, the theory and practice of medicine. The physiology symposium, spread over three days, was devoted to an exhaustive, many-sided analysis of the red-blood cell structure and function. Energetics, cell stability, and biochemical interrelations received outstanding treatment by workers drawn from many countries.

## Wildfowl Conservation Committee

SINCE 1954 the Nature Conservancy has held a regular series of informal meetings with leading wildfowlers and wildfowl conservationists, including representatives of the Wildfowlers' Association of Great Britain and Ireland, the Wildfowl Trust and the

British Field Sports Society. Much experience has been gained as a result of these meetings in bringing together the interests of conservationists and wildfowlers and about the selection and management of wildfowl refuges, such as those already set up on the Humber, at Southport and at the Caerlaverock National Nature Reserve. Wildfowl refuges form a desirable and, in some conditions, an indispensable means of conserving and increasing wildfowl stocks, in which the wildfowlers are no less interested than the protectionists and scientists. It is now intended to develop out of this consultation and agreement a National System of Wildfowl Refuges which will in due course form the main British contribution to the projected international network of European refuges. North America has long since operated such a system with outstanding success. The Conservancy has decided in view of the importance of the work of this informal group that it should now be formally constituted as the Wildfowl Conservation Committee with the status of a special advisory committee of the Conservancy. Mr. E. M. Nicholson, director-general of the Nature Conservancy, will be chairman of the Committee, which will include members of the Wildfowlers' Association of Great Britain and Ireland, namely, Lieut-Cmdr. J. W. Anderton, Mr. J. L. Hirst, Brig. G. D. Holmes, Colonel J. N. Vallance, Mr. E. L. Parish and Dr. G. W. Storey; the Wildfowl Trust, Mr. Peter Scott, Dr. G. V. T. Matthews, Mr. G. L. Atkinson-Willes and Mr. Hugh Boyd; the British Field Sports Society, Major J. G. Morrison, Brigadier A. H. Pepys and Sir Ralph Clarke; and the Nature Conservancy, Dr. J. Berry, Dr. E. B. Worthington and Mr. R. E. Boote. There are also two independent members of the Committee, namely, Colonel H. J. Cator and Major-Gen. C. B. Wainwright.

## Country Life

An interesting example of the fine work done by the Council for the Preservation of Rural Wales is described in its annual report for 1958–59 (Pp. 77+5 plates. London: Council for the Preservation of Rural Wales, 1960). In 1958, the late Lord Bledisloe, then president of the Gloucestershire branch of the Council for the Preservation of Rural England, offered to present a cup to be competed for annually for the best kept village in that county. Since then, many other competitions on a county basis have been held throughout England and Wales based on the Gloucestershire pattern. Some of these have been held under the auspices of various branches of these two councils, others under the auspices of other bodies such as women's institutes, county associations of parish councils, and rural community councils. In Wales, the competitions were inaugurated in Glamorgan through the award of the D. C. Jones Challenge Cup for the best kept Village in the Vale, under the joint sponsorship of the Council for the Preservation of Rural Wales, Glamorgan Branch, and the Barry Horse and Horticultural Society. Now there is a competition annually in most of the Welsh counties, and the entries are increasing every year. In the first year's competition, twenty-one villages entered and the prize was awarded to St. Nicholas, which was runner-up jointly with St. Fagans to St. Hilary last year. The report, available from the Secretary, Council for the Preservation of Rural Wales, 4 Hobart Place, London, S.W.1, contains full details of the many-sided activities of the Council in its work. The Council would welcome new members.

## *Archive for History of Exact Sciences*

In spite of the proliferation of scientific periodicals of all kinds, a warm welcome must be extended to the publication of a new journal, *Archive for History of Exact Sciences* (Vol. 1, No. 1. Pp. 106. Five numbers, individually priced, constitute a volume. D.M. 19.60. Berlin: Springer-Verlag, 1960). It should help in what has become almost an international duty, namely, to build those bridges possible between the domains of the sciences and the humanities. To do this is far from easy, but the need is a very real one. A study of the history of science is beneficial in both camps, always provided that it does not become merely a soft option; in other words, that the standards are set high. This, the new journal seems prepared to accept: it has a distinguished editorial board, and it will do well if it lives up to its dedication, "to uphold the tradition of P. Duhem and E. T. Whittaker". The first issue contains two papers—both dealing with important themes—one on rational mechanics in the Age of Reason, and the other on the beginnings of Euclid's axiomatic system. Contributions will be acceptable in the usual European languages, with the addition of Latin. To judge from the publisher's notice and the first of these articles, the English rendering leaves a good deal to be desired; the phrasing is a little clumsy and in one or two cases quite obscure. Improvement here should not be difficult, but it needs taking in hand at once, before this otherwise excellent production becomes suspect and its merits overlooked.

## Leather Manufacture

The inaugural lecture by Prof. A. G. Ward, following his appointment as professor of leather industries at the University of Leeds, was concerned with science and art in leather manufacture. Prof. Ward emphasized that, despite sixty years of intensive research, the making of leather still remains mainly an art and will continue to do so until its properties become amenable to measurement. At present there is little unanimity about what those properties are. In a brief historical review, Prof. Ward showed how much the improvement in the qualities of leather has been due to practical tanners who used methods analogous to scientific experiment but who lacked an accepted body of theoretical knowledge (Science and Art in Leather Manufacture: an Inaugural Lecture. Prof. A. G. Ward. Pp. i+20. Leeds: Leeds University Press, 1960. 2*s*. 6*d*.). Many efforts to provide the theoretical background to empirical facts have so far failed to provide an accepted and adequate view of leather-making processes. But the pace of change to-day makes it dangerous to the industry to assume that the art can develop fast enough to meet the challenge from industries based on science. Both the need of the industry and the state of the subject emphasize that an extension of basic science in this field is opportune. It is to be hoped that successful research can enable one more of the great craft industries of Britain to play its part in the modern world.

## Some Water-mites from Seepage Water

Collections by T. Gledhill from one locality yielded seven species of water-mites, each from a different family; four species are new to Britain and a fifth has previously been recorded from Ireland. The collections were made in seepage-water and are

outlined in the August issue of the *Journal of the Quekett Microscopical Club* (5, Ser. 4. No. 11. 1960). The locality is about 300 ft. above sea-level and situated on the eastern slopes of Claife Heights in the Lake District. The water appeared from under a large boulder, and made an area of wet woodland debris in some parts of which *Chrysoplenium oppositofolium* was growing. It was only when the surface debris was removed and a small hollow made that water would collect, and is the type of place which continental workers would call a helocrene. The species caught were: *A-Thienemannia schermeri; Hygrobates norvegicus; Hydrovolzia placophora; Panisellus thienemanni; Pseudofeltria scourfeldi; Bandakia concreta*; *Ljania bipapillata*. The first four were previously unknown in Britain, while *Panisellus thienemanni* is the only known species of its genus.

## Heterotrophic Nutrition of *Chlorella*

In studies of the heterotrophic nutrition of *Chlorella vulgaris* (Brannon No. 1 strain) cultured in darkness, D. J. Griffiths, C. L. Thresher and H. E. Street (*Ann. Bot.*, N.S., **24**, 1; 1960) have tested the utilization, as carbon sources for growth and respiration, of a range of sugars, sugar alcohols, sugar phosphates, organic acids and monohydric alcohols. Considerably higher rates of growth and respiration were obtained with *d*-glucose than with any other substance tested. Ethanol (at 0·005 *M*) sustained both growth and respiration at *c.* 50 per cent of the level with glucose (0·028 *M* or higher). Evidence was obtained that the organism can become 'adapted' to utilize *d*-galactose and sucrose as effective carbon sources. Sustained growth was not obtained with any of the other substances tested. The glucose monophosphates, methanol and certain organic acids (oxalacetate, α-ketoglutarate, *cis*-aconitate, and pyruvate) clearly stimulated oxygen-uptake, but to a less extent than ethanol. The other substances tested were either inhibitory to respiration or inactive, or of very low activity as substrates. The growth in darkness and in liquid culture of *Chlorella* when supplied with *d*-glucose was insensitive to *p*H over the range 4·5–7·0, and was markedly enhanced by a high level of aeration. Gains in cellular dry weight ranging from 45 to 90 per cent of the weight of *d*-glucose disappearing from the culture medium were recorded in growth experiments; measurements of evolution of carbon dioxide in the Warburg apparatus indicated retention of up to two-thirds of the glucose–carbon in cell material.

## Christmas Lectures for Young People

Among the lectures which are to be specially organized for young people during Christmas and the following weeks are: The one hundred and thirty-first course of six Christmas lectures, which is to be given by Dr. V. E. Cosslett on "Seeing the Very Small", at the Royal Institution on December 29, 31, January 3, 5, 7, 10, at 3 p.m. (Further information can be obtained from the Royal Institution.) A lecture on "Plastics and Textiles", to be given by Dr. H. A. Thomas in the Lecture Theatre of the Institution of Electrical Engineers, Savoy Place, London, W.C.2, on January 2, at 2.30 p.m. (Further information can be obtained from the Plastics Institute, 6 Mandeville Place, London, W.1.) A lecture on "Gyroscope and Pendulum—the Modern Travel Agents", to be given by R. J. Lees, head of the Instrument and Photographic Department of the Royal Aircraft Establishment, in the Lecture Theatre, Royal Aeronautical Society, 4 Hamilton Place, London, W.1, on January 5, at 3 p.m. (Further information can be obtained from the Royal Aeronautical Society.)

## Announcements

Prof. W. Hume-Rothery, Isaac Wolfson professor of metallurgy in the University of Oxford, has been elected an Honorary Member of the Institute of Metals. Major C. J. P. Ball, Dr. Maurice Cook and Lieut.-Colonel S. C. Guillan have been elected Fellows, in recognition of the services that they have rendered to the Institute. The total number of Honorary Members and Fellows are each restricted to twelve.

Prof. Alan Wood, professor of geology at the University College of Aberystwyth, has been awarded the Silver Medal of the Liverpool Geological Society in recognition of his contributions to geology.

Prof. V. F. Weisskopf has been appointed director-general of CERN, in succession to Dr. J. B. Adams, who will, next year, return to the United Kingdom as director of the Culham Laboratory for Plasma Physics Research. Prof. Weisskopf has been at the Physics Department, Massachusetts Institute of Technology, since 1945.

Brigadier H. E. Hopthrow, assistant secretary to Imperial Chemical Industries, Ltd., has been elected secretary of the Royal Institution, in succession to the late Sir Harold Spencer Jones.

The Television Society has invited Sir Harold Bishop, director of engineering of the British Broadcasting Corporation, to become president in succession to the late Sir George Barnes. Sir Harold Bishop has been with the Corporation since it was the British Broadcasting Company, Ltd., in 1923. He has been director of engineering since 1952.

Biographical material relating to the late Academician A. F. Joffe is being collected by Madame Joffe. Any letters, photographs or personal recollections would be welcomed and should be sent to Madame Joffe at the Institute for Semiconductors, Kutuzova 10, Leningrad *D*-187, U.S.S.R.

A symposium on "Light Metal Industry in India" is to be held in the auditorium of the National Metallurgical Laboratory, Jamshedpur, during February 14–17, 1961. Further information can be obtained from the Director, National Metallurgical Laboratory, Jamshedpur-7.

The fifth international conference on "Ionization Phenomena in Gases" is to be held at Munich during August 28–September 1, 1961. The conference is being organized by the Verband Deutscher Physikalischer Gesellschaften. Further information can be obtained from the Secretariat, Fifth International Conference on Ionization Phenomena in Gases, Oskar-von-Miller-Ring 18, Munich 1 (P.O. 463).

A Supplement (1957–1959) to the Catalogue of Lewis's Medical, Scientific and Technical Lending Library has now been published (Pp. 306. To subscribers to the Library, 5*s.* net. London: H. K. Lewis and Co., Ltd., 1960. 10*s.* 6*d.* net). It is arranged alphabetically by authors, and is provided with a classified subject index which gives the names of authors of books listed in the Supplement which deal with the subjects classified.

# CITY OF LIVERPOOL COLLEGE OF TECHNOLOGY

## NEW SCIENCE BLOCK

SIR David Eccles, Minister of Education, opened the first instalment of the new City of Liverpool College of Technology on September 30, 1960. The new building provides accommodation for the Departments of Chemistry and Biology, Physics and Mathematics, and Pharmacy. The building (Fig. 1) has been designed and the work carried out under the direction of Dr. Ronald Bradbury, city architect and director of housing. It has been erected by Messrs. Henry Boot and Sons, Ltd., of Bootle, at a cost of £310,500. It is a concrete cased steel-framed structure, faced with rustic brickwork and artificial stone, purpose made bricks and coloured tiles forming patterned infilling panels between the floor-levels on the front elevation. The various floors, formed with precast concrete flooring units, have been finished generally with thermoplastic floor tiling, which in the case of the laboratories is acid resisting. Particular attention has been given to the design of the specialized laboratory furniture and fittings, which incorporate drawer and storage units and which are interchangeable, the whole of the units being finished in acid-resisting lacquer. The various services to the laboratories, which include hot and cold water, gas, electricity, compressed air, vacuum, steam, etc., are concealed in vertical and horizontal ducts, as well as in the suspended ceilings. The latter are formed with rectangular panels of asbestos board, and the patented system of suspension enables each panel to be removed easily when access to the various services is desired. Each floor is served by an automatically electrically operated passenger and service lift, the latter enabling stores and materials to be transported conveniently from the main store on the ground floor to the materials issue stores on the upper floors. The laboratories have been designed, so far as possible, to house the most modern equipment and apparatus for teaching and research work in the departments concerned.

The Department of Chemistry and Biology occupies the ground and first floors, with certain advanced-research laboratories located on the second floor. The remainder of the second floor and the whole of the third floor accommodate the Department of Physics and Mathematics. The Department of Pharmacy is accommodated on the fourth floor, and a range of animal houses and ancillary rooms has been provided on the main roof. Each department has appropriate types of laboratories, rooms for departmental heads and staff, classrooms, lecture theatres and store rooms. The Department of Chemistry and Biology provides full professional training, postgraduate work and research for chemists and biologists, including courses leading to the external B.Sc. degree of the University of London, the diploma in technology in applied chemistry, and graduateship of the Royal Institute of Chemistry.

Fig. 1. New Science Block, City of Liverpool College of Technology

The Physical Chemistry, and Inorganic and Organic Laboratories are well equipped for teaching purposes. The Organic Research Laboratory includes apparatus specially designed by the staff for research work on gas adsorption, gas chromatography and electrochemistry. The equipment provided in the Instrumental Laboratory includes a recording polarograph, emission spectrograph, and an argon chromatograph. Some important and costly pieces of equipment have been installed in the special laboratories on the second floor. These include a Phillips E.M.100 electron microscope giving a resolution of 20-15 Å., and is being used in conjunction with an Edwards '12 E 6' coating unit for the examination of various inorganic gels and precipitates; a 'Raymax 60' X-ray generator, which is being used for X-ray powder photography, and a 'Unicam S.P.100' infra-red spectrometer. A suite of rooms is provided for research work in radiochemistry and radiobiology.

The Department of Pharmacy is responsible for the training of pharmacists who will eventually take their place in hospitals, manufacturing industry and retail work. Students attend the pharmaceutical chemist qualifying course. The Dispensary provides all the facilities required for modern dispensing. The Pharmaceutical Chemistry Laboratory is fully equipped to deal with standard analytical and preparative procedures with a particular bias to semi-micro techniques. Specialized apparatus includes a spectrophotometer, electrophoresis tank, a polarograph and Karl Fischer apparatus. The accommodation includes the Pharmacology and Physiology Laboratory and the Aseptic Laboratory, which enables students to work under conditions designed to exclude bacterial and fungal contamination from the air. The small-scale manufacturing laboratory permits many large-scale processes to be duplicated accurately. The research laboratories (situated on the second floor) are used for investigations covering pharmaceutical subjects, using modern techniques and apparatus.

The Department of Physics and Mathematics provides courses leading to the National Certificate in Applied Physics and to graduateship of the Institute of Physics, and examinations for external degrees of the University of London. The Department is also responsible for the mathematics and physics classes required by other departments for their certificate, diploma, and Diploma in Technology courses. Postgraduate courses are provided, and the Department has organized a number of research projects. The Physics Laboratories are well equipped and include spectrographic apparatus, high-vacuum equipment and an electron-microscope, the latter being a gift from an industrial concern. A large differential analyser has also been presented to the Department by an industrial firm. For the courses in mathematics and statistics there are various calculating machines, and an analogue computer is to be built.

Research projects undertaken by the Departments accommodated include the following: chromatography, electrochemistry, inorganic, polymer, sugar, surface and radiation chemistry, X-ray diffraction, electron microscopy; electron magnetic resonance, examination of cosmic dust, numerical analysis, and pharmaceutical subjects. A considerable amount of research work is carried out in collaboration with various industrial organizations. A number of members of staff have qualified for research grants from the Department of Scientific and Industrial Research.

Departments of the College offering professional courses award College associateships (A.C.T. (Liverpool)) to students who have satisfactorily completed courses approved for this purpose by the Board of Studies. Full-time and 'sandwich'-course students may be awarded an honours associateship, and, in exceptional cases, only students completing approved part-time courses. The College fellowship (F.C.T. (Liverpool)) is awarded for approved research work carried out in the College. S. A. J. Parsons

## CROYDON TECHNICAL COLLEGE

A NEW building, which was opened by H.M. the Queen on November 2, houses Croydon Technical College, Croydon College of Art and the Denning Hall. The premises, which occupy a site of nearly four acres, were projected before the War, but construction had to be deferred, and work was not begun until 1953. Although it has been dealt with in three stages under three separate contracts, building work has been going on continuously from 1953. The total cost of the building is about £1,450,000 and of the equipment housed in it about £375,000. The provision made will be enough for some 500 full-time and 10,000 part-time students. The architects are Messrs. Robert Atkinson and Partners, of Manchester Square, London, W.1.

Croydon Technical College traces its ancestry back to the establishment of classes, mainly in scientific subjects, in 1838, when the Croydon Literary and Scientific Institute was founded. But possibly a more important occasion was the foundation of a scheme for technical classes for artisans by the Rev. Oakley Coles, curate of the Croydon Parish Church, in 1888. Two years later the Croydon Council decided to set up the Polytechnic, based on this modest beginning, and a new building was opened by the then Archbishop of Canterbury, Dr. E. W. Benson, in December 1891. As this was some years before the establishment of the local education authority, the Polytechnic was in fact the first educational institution to be maintained by the Council and is also the oldest technical institution to be maintained by any Council in the Greater London area. Control of the Polytechnic was transferred to the new Education Committee in 1903. The work of the College was extended continuously until, in 1929, H.M. Inspectors reported that the old building was inadequate for the services which the College was providing. Expansion of the work of the College has continued for the past thirty years, and recently the number of student enrolments has been increasing annually by at least 10 per cent. The expansion of the work since 1945 has in fact been greater than during the whole history of the College before that date. Enrolments for the present

session total 450 full-time and 8,000 part-time students.

The six-storey building consists of a centre block housing the administrative offices, refectory, laboratory and gymnasium—facilities shared by both the Technical College and College of Art—and four wings. The two west-wings and the majority of the south-east wing provide accommodation for the Technical College, while the north-east wing is exclusively for the College of Art. Noisy workshops used for mechanical engineering and building have been placed at the lower-ground floor-level, with special construction to keep noise and vibration from affecting the quieter rooms above, while a service road for these workshops runs under the whole length of the building. Lecture rooms, drawing offices and the lighter laboratories and practical rooms for science, electrical engineering, commerce, domestic science and food trades are grouped on the floors above. Lifts and the main staircases situated at the junctions of the two west wings and the two east wings communicate with all teaching floors; other staircases are provided at the extreme ends of the four wings. In the courtyard between the two east wings is situated the Denning Hall, which will seat approximately 750, and is a gift to the town by Mrs. Elizabeth Denning, in memory of her husband, who was Mayor of Croydon during 1913–16. This fine Hall may be used for the purposes of both Colleges and for other public purposes with an educational association.

Space will permit the detailed description of one Department of the College only, and the Department of Science has been chosen. This Department occupies almost all the fourth-storey accommodation of the two west wings and the centre block. The south-west wing provides laboratories for inorganic, organic and physical chemistry together with balance, store, preparation and dark rooms, a lecture theatre and classrooms. Physics is housed in the north-west wing, and is provided with four laboratories, a workshop, dark room, a lecture theatre, classrooms and stores. Also in this wing is the radioisotopes suite with the X-ray room adjacent. In the centre block on this floor are general science and biology laboratories together with further class-rooms. This accommodation serves the following courses of study:

| | Students |
|---|---|
| Full-time | |
| General Certificate of Education | 125 |
| Part-time (day) | |
| General Certificate of Education | 112 |
| B.Sc. (General) | 38 |
| Ordinary National Cert. in applied physics | 43 |
| Higher National Cert. in applied physics | 43 |
| Graduateship of Institute of Physics | 9 |
| Ordinary National Cert. in chemistry | 57 |
| Higher National Cert. in chemistry | 20 |
| Evening | |
| General Certificate of Education | 248 |
| Horticulture | 17 |

In addition, the Science Department acts as a 'service' department by undertaking the teaching of science required by other Departments of the College, for example, Bakery Science.

To provide for unknown expansion in the future, the building is designed on a unit grid with external planning and services as flexible as possible. In the chemistry section, for example, the larger class-rooms on the opposite side of the corridor to the existing laboratories are already provided with floor ducts and connexions to existing services to permit them being converted readily into extra laboratories. This means that, if additional building is needed, it will be principally class-room accommodation and that the dispersal of the various kinds of departmental practical rooms will be avoided.

Many new technical colleges cater for future expansion by building different blocks for different purposes, each of which has a 'growing point' for extensions. This method may be simpler than that described above; but the Croydon plan, with 'growing points' for class-room accommodation available on the inner sides of the existing east wings, is likely to provide the more compact building with shorter lines of communication for its users.

The integral nature of the building and the decision to place two independent Colleges under one roof are perhaps the most distinctive features of what the Queen referred to as "this imaginative experiment" in which young scientists, technicians, craftsmen and artists may "meet and exchange ideas with those trained in other fields of knowledge".

## BIOLOGY OF SPACE TRAVEL

A SYMPOSIUM on the "Biology of Space Travel", organized by the Institute of Biology, was held during September 29–30 at the Royal Geographical Society, Kensington.

For the opening session the chair was taken by Sir Lindor Brown. The first paper was by Air-Commodore W. K. Stewart, of the Royal Air Force Institute of Aviation Medicine, Farnborough, who gave an account of recent work on the physiological effects of acceleration. A semi-recumbent posture would allow acceleration for several minutes at about eight times gravity without severe physiological disturbance, and the accelerations on take-off of rockets would be close to this figure. However, little is known about the effects of vibration and of emotional disturbance under such conditions, and in such high accelerations the astronaut would find it very difficult to carry out any movements other than movements of the eyes and of the supported hands. The forces on re-entry would probably reach rather higher figures, in the region of ten times gravity, and provision would be needed for ensuring that the astronaut was correctly positioned in relation to the deceleration; if this were assured the forces would be tolerable for the short period expected. Wing-Commander T. C. D. Whiteside, also of the Royal Air Force Institute of Aviation Medicine, followed with a paper on the effects of the gravity-free state. Although no data are available for man for prolonged periods of weightlessness, it is probable that the physiological effects would not be severe. Eating would be easy, but fluids would have to be sucked from plastic containers. Locomotion would be easy in the dimensions of a small space-vehicle. However, it seems likely that muscular weakness would develop in a few days due to lack of exertion in a weightless environment, and this might reduce the tolerance to deceleration on re-entry. Regular exercises would

be needed to combat this problem. An unsuspected difficulty in low gravitational fields might occur if artificial gravity was produced by rotation of the space-vehicle itself, since even in large vehicles the Coriolis forces in the labyrinth of the ear produced on moving the head might give rise to disabling giddiness.

Lieut.-Colonel W. R. Turner, of the United States Air Force Aerospace Medical Division, Ohio, described the exacting series of physical and psychological tests employed in selecting candidates for the "man-into-space" projects such as "Project Mercury". The candidates were chosen from men with high basic qualifications, including a degree in engineering and 2,000 hr. of piloting jet aircraft. The examinations included exhaustive medical and psychological examinations and tests under conditions simulating those anticipated in space flight, such as high temperatures, acceleration and vibration. Other tests estimated noise-tolerance, patience with complicated and confusing machinery, and the ability to tolerate long periods of isolation. It was found that, given a normal physique, the motivation of the candidate played a surprisingly large part, and keen but level-headed men of about thirty-five years were the most successful at these tests.

For the second session the chair was taken by Sir Solly Zuckerman. Dr. D. McK. Kerslake read a paper by Flight-Lieutenant J. Billingham, of the Royal Air Force Institute of Aviation Medicine, on the maintenance of the thermal environment in space vehicles. When in orbit the temperature of the cabin would be maintained at a comfortable level by fairly simple air conditioning together with suitable insulation of the walls. On re-entry, however, the frictional heating of the exterior might cause severe over-heating of the interior, particularly if the time for descent was prolonged for any reason. Whether such over-heating will cause skin burns or heat stroke will depend largely on the rate of the rise in temperature. Both these dangers can be avoided by a special suit in which cold air is piped to the skin, and some impressive experiments were cited in which a man was well protected for several hours by this means in an environment at 125° C.

Mr. N. W. Pirie, of the Rothamsted Experimental Station, Harpenden, discussed the problem of the synthesis or re-cycling of oxygen, food and water on longer space flights. Water is unlikely to be a severe problem since most of the expired water vapour can be readily condensed and distillation of urine would allow the recovery of most of the remainder. The astronaut would require about 1 kgm. of oxygen a day, and the expired carbon dioxide would have to be absorbed: for short voyages potassium tetroxide would be suitable for this dual purpose. For longer voyages it has been suggested that algae such as *Chlorella* could be used to regenerate oxygen and foodstuffs by photosynthesis. There would be many technical problems in this. Outside the orbit of Mars the intensity of sunlight would fall to a level too low for effective photosynthesis: the algae would be very difficult to handle, maintain and process, and they would not in any event be suitable as the sole source of food. Complex chemical re-syntheses would require weighty and complex apparatus. An exciting possibility is that some way may be found of readily converting energy into essential biochemical intermediates, so that one could 'recharge' one's energy supplies in a manner analogous to recharging an electric accumulator.

Mr. S. W. F. Hanson, of Armour and Company, Ltd., London, read a paper on the supply of food to astronauts. He described recent progress in packaging food in a suitable form, and in particular the advantages for long journeys of dehydrated and pre-cooked foods, which can be prepared in wide variety; this is of great importance from the psychological point of view. He believed that at the most *Chlorella* would prove to be only an adjunct to the diet of astronauts, even if the technical problems of growing it were overcome. He showed a film which illustrated some of the problems of feeding under conditions of weightlessness.

On the morning of the second day of the symposium Sir Harrie Massey took the chair. Dr. P. Alexander, of the Chester Beatty Research Institute, London, read a paper on radiation in space and its effects on man. Most of the ionizing radiation in space consists of electrons and protons. The majority of the electrons will be stopped by the walls of the space-vehicle, though they will generate X-rays in this process which could penetrate the vehicle; in the inner of the two equatorial Van Allen radiation belts this secondary radiation might deliver a dose of about 5 rads/hr. to the astronaut. The protons, although more penetrating than electrons, would only deliver about 1 rad/hr. The radiation in the outer Van Allen belt would be less than that in the inner belt. In deep space the dose-rate would be small, probably about 10 rads per annum. In a short flight through the Van Allen belts and back the astronaut would receive a total of about 15–20 rads, which would be well below the permissible level in these special circumstances, and, by choosing a polar route, the radiation would be reduced considerably.

A paper on the psychological problems of solitude and confinement was read by Dr. R. Beech, of the Institute of Psychiatry, Maudsley Hospital, London. Dr. Beech reviewed thoroughly the published research on this topic, and concluded that very little reliable data were available. The tendency for sensory deprivation to cause abnormal mental behaviour, such as hallucinations, was now well recognized, but the degree to which this might occur in space flights was problematic, and little was known on the best ways to combat it. Dr. W. Grey Walter, of the Burden Neurological Institute, Bristol, in a communication entitled "The Human Brain in Space Time", described some recent work on the ability to learn under difficult and confusing conditions, and he emphasized the marked individual variations in the ease with which certain associations were recognized and learnt. He also raised the interesting question of the mental qualities which would be most desirable in astronauts, and noted that outstanding pioneers in many fields have frequently been decidedly eccentric individuals.

The chair in the final session was taken by Dr. A. S. Parkes, president of the Institute of Biology. Dr. P. H. A. Sneath, of the National Institute for Medical Research, London, discussed the dangers of contaminating the planets with terrestrial micro-organisms, or of contaminating the Earth with planetary organisms, should these exist. Recent work suggests that some soil bacteria may be able to multiply under the conditions found on Mars, and if we contaminate Mars with such bacteria the loss of scientific information would be enormous. The sterilization of a space rocket poses some very difficult problems, which urgently need further attention. It would be very dangerous to bring back to the Earth samples from other planets, because of the

risk that they might contain organisms which could prove dangerous to the ecology of the Earth, and it would be advisable first to carry out experiments on these in closed ecology chambers on manned satellites.

The last paper was by Dr. Harlow Shapley of the Harvard Observatory, who discussed the probable environment of other planets. He felt sure that there must be many planets in the universe which would be suitable for life as we know it on Earth (quite apart from the possibility of life in other forms) and it would seem inevitable that some form of life would have evolved on many of them. Whether we can ever communicate with such worlds was another matter. An important factor in the evolution of higher life may be the ozone layer of the Earth's atmosphere (itself due indirectly to the photosynthetic production of oxygen by primitive plants) since this layer protects terrestrial organisms from short-wave ultra-violet rays. None of the other planets of our solar system appears to possess such an ozone layer.

In summing-up, Dr. Parkes discussed the possibility that astronauts might travel for most of their journey in a state of suspended animation, only to be revived when they reached their destination, and recent work on the freezing of whole animals shows that this is not a wholly fanciful suggestion. This also raises the question of whether man would have a useful part to play in the early stages of space travel, or whether it would be better to devise very elaborate machines to make the observations. The symposium had the excellent result of bringing together workers in many disciplines, and it showed that the remaining difficulties in short-range space flight were mainly engineering problems, while those affecting the astronaut himself would soon be largely solved.

## INFLUENCE OF CLIMATE ON LIFE

ONE of the most obvious, and at the same time one of the most neglected, statements in the whole field of biology is that all life depends on its environment. Biologists and medical men of the past have made this the basis of much of their thinking, and engineers and architects have often built machines or houses to suit specific climates, but scientific journals still contain reports of biological experiments in which the experimental conditions were neither controlled nor recorded, and buildings or vehicles often fail to display any consideration for local climate. Even the impressive Unesco headquarters completed a few years ago in Paris are liable to cause heat exhaustion in people working there on sunny days, and it is well known that motor-cars are the hottest places to be found in many tropical countries.

At the other extreme, tables of comfortable environmental temperatures usually assume that simple mathematical expressions can be valid in biological processes, and ships ply through some of the climatically most pleasant seas of the world carrying with them the same constant artificial micro-climate which can be found in any office building in New York or London.

The International Society for Bioclimatology and Biometeorology held its second International Bioclimatological Congress recently in London with the avowed intention of improving knowledge about the influence of climate on life by bringing together people active in all parts of the world and in all branches of science whose work is related in some way to these problems. The success of the Congress was considerable, and its effects will probably be felt for some time to come. Some of the work helped to cross-fertilize or to dispel misconceptions by passing ideas and techniques between different specialties or different countries, but much new information of interest was also provided.

Symposia included one on life at high altitudes in which Prof. R. Margaria (University of Milan) related the problem of acclimatization to anoxia with space flying where less oxygen means less pressure which, in turn, means less weight. He also reported the results of experiments which showed that the carotid body chemoreceptors of man were sensitive to oxygen, in any event during anoxia, which was of interest in view of occasional criticisms against conclusions made from such studies on anæsthetized animals. A paper by Prof. A. von Muralt and Dr. W. H. Weihe (University of Berne) reported experiments carried out on the Jungfraujoch at about 11,000 ft. and mean barometric pressures of about 500 mm. of mercury which showed that the threshold for various stimuli, such as taste, touch or tendon reflexes, was reduced at high altitudes but returned to normal if oxygen was breathed in. Prof. R. Schumacher and Dr. R. Schindler (Hamburg) reported on the 'high-altitude disease' observed at about 16,000 ft. in the Andes, where cattle developed heart failure and œdema but recovered quickly after a descent of only about 1,500 ft., a condition reproduced experimentally in rats and observed sometimes in man. It is difficult to escape the conclusion from this that the pressures to be chosen for long journeys into space will not be the lowest to which people at rest can become acclimatized but the lowest which will avoid heart failure and œdema.

In a symposium on life in the tropics, Prof. Alrick B. Hertzman (University of St. Louis) suggested, among other things, that correlations between the cardiac output and the skin blood-flow were purely coincidental, as there were situations when one was high and the other low, for example, when the skin is cooled after the whole body has been warmed. However, it could equally be argued that the correlations between these are part of a system integrating many variables, which usually works in a given way but in which no single correlation is immutably fixed, thus conforming to what might be predicted in any complex control system and making the relationship between cardiac output and skin blood-flow somewhat more predictable than a mere coincidence. Dr. H. Boyko (Israel) showed some impressive photographs to illustrate how a patch of desert could be turned in a very short time into a lush garden by applying sound principles of bioclimatology. Dr. J. C. D. Hutchinson (now in Parramatta, Aus-

tralia, but well remembered from his Cambridge and Edinburgh days) surveyed the problem of domestic cattle in the tropics, especially from the point of selective breeding, and he showed, among other things, how clipping the fur could increase the rate of growth in farm animals, simply by improving heat tolerance. Prof. W. Richards (Bangor) discussed tropical plants, and he quoted recent evidence from Ibadan and Cambridge that the rapid growth of these plants was related to the favourable growth of their new leaf. He also quoted some odd rhythms in equatorial plants, for example, one in Singapore which has a rhythm of 2 years and 8 months, or the Malayan pigeon orchid which flowers quite irregularly though pigeon orchids in any given area always flower on the same day.

Prof. C. P. Luck (Kampala, Uganda) described his studies on elephant, giraffe, rhinoceros and buffalo, which he hunts with cross-bows and succinyl-cholin-impregnated arrows, so that he can collect sweat, blood and urine, measure body temperatures, or even inoculate animals against diseases, without harm to the animals and, one was glad to hear, with safety to himself. Prof. E. B. Edney (Salisbury, Southern Rhodesia) showed that crabs took increasing amounts of oxygen and survived greater temperatures after acclimatization to heat than before, and that tsetse flies were able to evaporate water from their spiracles, thus avoiding over-heating while engaged in the hard work of sucking blood in close proximity to a warm animal.

There were many small sessions dealing with more specialized problems. Dr. T. R. A. Davis and Dr. R. J. T. Joy (U.S. Army Research Laboratories, Fort Knox) reported that animals and man exposed to cold for 2 hr. daily showed a reduction of shivering after 21–24 days, which was accompanied by an increase of heat production in the muscles without any electromyographic evidence of shivering. Prof. J. Grayson (Ibadan, Nigeria) produced evidence of similar, apparently purely chemical, heat regulation in the liver, which could also play a part in improved cold tolerance after acclimatization to cold. Related to these findings were those of Prof. H. Hensel and his associates of Marburg, Germany, that cooling of the hypothalamus in animals produced an increase of metabolism in the rest of the body within a few seconds, but more so at lower than at higher environmental temperatures. Taken together, these data probably mean that there may exist a form of true chemical heat regulation not related to shivering, which is probably controlled by the temperature of the hypothalamus, and which can be modified either by thermal impulses from the skin or by a repetition or continuation of the cold stimulus.

Equally interesting was evidence, also from Prof. Hensel, that thermal receptors discharge at a constant level of activity during constant stimulation, so that in the absence of any environmental change the central nervous system receives a constant level of thermal information. In other words, thermal receptors would seem to become adapted extremely slowly or not at all. This fits in well with evidence from the London Hospital Medical College that the diminution of sensations and responses to repeated or continued stimuli which plays an important part in acclimatization is a result of a central nervous mechanism of habituation and not of any changes in the peripheral receptors.

Other discussions had a wide range, though some did not get beyond defining useful fields for further study. Among these was the problem of air pollution, which appears to be complicated by the fact that certain particles suspended in the air reinforce the action of others. Recognition of one or more potentially harmful substances in the air is therefore insufficient to assess air pollution, and predictions may have to be based on a better knowledge of synergistic actions of individual particles.

Difficulties of using scales of environmental comfort were stressed in a very active group on town planning under the chairmanship of Prof. J. K. Page (Sheffield). It appears that builders and engineers use at least four different comfort scales; but if one remembers the effects of habituation on thermal comfort it appears likely that many more comfort scales would be in use if more people had tried to compute such scales. Evidence was presented also that the provision of warmth is cheaper and easier in cold climates than the provision of cool air in hot places; but this may not always be so, as civilized communities have studied heating longer than cooling. Evaporating water, where it is available, from the roofs of buildings, as well as the use of solar energy to drive cooling compressors, might lead to simple and cheap ways of avoiding the overheating of buildings or vehicles in hot climates, and considerable improvements may be achieved by good design. Opinions were expressed suggesting that technology may soon remove the need for any physiological adjustments to changes of temperature, but by and large this Congress left the impression that we are still far from the days when uniformly clad people will live at a constant level of thermal acclimatization in one and the same environment anywhere on the Earth and outside it.

E. M. Glaser

## COLONIAL DEVELOPMENT AND WELFARE

THE schemes made under the Colonial Development and Welfare Act in the period April 1, 1959, to March 31, 1960, which are detailed in the latest return, bring the total commitments, from April 1, 1946, under the Act to £221,023,632, of which £18,792,837 is for research schemes*. The totals for the year in question are £33,001,222 for development and welfare and £2,370,261 for research schemes. Of this last, £1,009,974 is for agriculture, £560,600 for pesticides, £375,080 for medicine, £167,180 for locust control, £63,860 for fisheries, £57,289 for products research, £45,160 for tsetse fly and trypanosomiasis research, £41,697 for social science, and £7,796 for economic research.

Of the actual research schemes, £313,032 is for the Colonial Pesticides Research Unit, Arusha, Tanganyika, as well as a supplementary £57,139, 1960–

* Colonial Development and Welfare Act. Return of Schemes made and of Loans approved under the Colonial Development and Welfare Act in the Period from 1st April, 1959, to 31st March, 1960. Pp. 50. (London: H.M. Stationery Office, 1960.) 2s. 6d. net.

63; £181,000 for the agricultural research services, North Borneo, with a further £73,625 for the establishment of agricultural research stations; £124,755 for the Regional Research Centre at the Imperial College of Tropical Agriculture, Trinidad, and £47,459 for herbicides research at that College; £69,500 for the Anti-Locust Research Centre and its extra-mural activities, 1960–61; and £51,009 for the Colonial Pesticides Research Unit, Porton, 1960–63. £47,892 went to the East African Agriculture and Forestry Research Organization, £33,504 to the East African Trypanosomiasis Research Organization, and £33,283 to the East African Veterinary Research Organization; £38,250 was for trials with anti-typhoid vaccines; £55,506 to the Wellcome Institute for research on foot-and-mouth disease; £57,295 to the West African Rice Research Station, Rokupr, 1960–61; £77,911 for improvement and extension of agricultural facilities, Sarawak; and £33,350 for the study of dental leishmaniasis, British Honduras.

Other major research schemes include a supplementary £17,174 to the Fish Culture Research Institute, Malacca; £18,503 for research on spraying techniques and trace element deficiencies at Long Ashton; £42,968 for trachoma research in London and in The Gambia; £25,920 for the Desert Locust Survey; £16,607 for research into farm production costs, Kenya; and £39,650 for cereals research, Kenya, as well as £21,235 for research on coffee berry disease there, 1960–62; a supplementary £20,153 for cotton pest research, Nyasaland; £22,930 for the Joint Fisheries Development and Research Unit, Sierra Leone, 1960–62; a supplementary £19,489 for the Colonial Microbiological Research Institute, Trinidad; and £15,126 for the East African Virus Research Institute; £27,882 was for the Colonial Pesticides Information Service, 1960–64; £16,500 for Overseas Research Fellowships, 1960–64; and £15,000 for Colonial Medical Research Studentships, 1960–64.

Development and welfare schemes of scientific interest include £17,232 to the Overseas Geological Surveys for age determination of rocks at the Geological Museum, University of Oxford; £25,930 for the Desert Locust Survey; grants totalling £376,633 to the Agricultural Department, Kenya, for the intensification of African agriculture, 1958–59; a supplementary £74,974 to Somaliland for scholarships and training abroad; £182,000 for the establishment of a Nature conservation area in the Ngorongoro Crater Highlands, Tanganyika; £68,500 for intensified control in Tanganyika of the Sudan dioch (grain-eating birds); and a supplementary £157,685 for forestry development, British Honduras. Educational grants include, besides £250,000 for a student hostel block, University College, Ibadan, Nigeria, a number of grants totalling more than £169,000 to the Nigerian College of Arts, Science and Technology; £210,000 and £233,250 for the second and third phase, respectively, of the expansion of general education in Lagos; £308,120 for building of schools in Northern Nigeria (with £341,500 for the development of health services); £368,000 to Fourah Bay College, Sierra Leone, for constructing and equipping two halls of residence, as well as £360,000 for the construction and equipment of Freetown Teacher Training College, Sierra Leone, and miscellaneous grants totalling more than £780,000 to the University College of the West Indies.

## CONTROL OF INFECTIONS

DUE mainly to vaccination, fewer persons now suffer or die from such diseases as diphtheria, poliomyelitis and tuberculosis. If immunization programmes using the best available vaccines were more generally applied, the risk of infection from certain diseases could still further be reduced. Some of the problems raised by vaccination procedures are discussed in a recently published report of a European Technical Conference on the Control of Infectious Diseases through Vaccination Programmes*.

The report gives a broad picture of the legislation in force regarding vaccination in Europe. Compulsory vaccination varies considerably from one country to another; many use a mixed system in which some vaccinations are compulsory while others are not, and the general tendency is to substitute effective health education for compulsion by law. An important aspect is that of inspection and the recording of vaccinations, which makes it possible to obtain reliable data regarding their effectiveness. Generally the cost of vaccination programmes is borne by the health authorities; in some cases the cost has to be met by the patient himself, which may adversely affect the success of the campaign.

The report gives a brief account of the value and present state of the most important vaccinations. Although smallpox does not exist as an endemic disease in European countries, it was generally felt that it was still necessary to maintain a relatively high level of immunity in the population through continued vaccination programmes. It was agreed that BCG vaccination should be considered as part of the over-all tuberculosis control programme of any country. The report discusses the types of anti-polio vaccines used at present; inactivated virus vaccine and attenuated live virus vaccine, which have been successfully applied in the Soviet Union to more than twelve million persons. The use of triple vaccine against diphtheria, tetanus and pertussis is recommended, and consideration is given to the suitability and effectiveness of many other vaccines, such as those against influenza, typhoid, paratyphoid, tularæmia, brucellosis, rabies, etc., as well as those used against quarantinable diseases (yellow fever, typhus and cholera).

After dealing with the risks and techniques of different vaccinations, the report discusses the importance they may have in the control of infectious diseases. It finally suggests models for programmes which, in the opinion of the conference, might be adopted in the various countries according to the degree of development of their health services and their own particular problems.

* World Health Organization. Publication No. 198: European Technical Conference on the Control of Infectious Diseases through Vaccination Programmes, Rabat, Morocco, 23–31 October, 1959. Pp. 21. (Geneva: World Health Organization; London: H.M. Stationery Office, 1960.) 1 Swiss franc; 1s. 9d.; 0·30 dollars.

# OPTICAL IMAGE ASSESSMENT

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IN recent years considerable attention has been devoted to developing methods for assessing optical image quality. A realistic criterion for the performance of optical systems has long been sought, and the advent of communication theory in optics has brought forth the concept of frequency response[1-4]. The relative merits of conventional testing methods such as the star test, the square wave or bar test chart, edge response, energy density in the point image and the like have been adequately discussed. However, it is not widely recognized that for incoherent illumination all these criteria are simply interrelated and derivable from the basic point spread function of the optical system.

The need to assess the image quality of a lens system arises, first at the lens design stage, when the designer is forced to make compromises in order to balance the residual aberrations in the optical system, and secondly, when the lens is at the construction and assembly stage. The lens designer would like to estimate the information transfer characteristic of the system under its true operational conditions. Here the effects of aberrations, diffraction, contrast of the object domain, air turbulence and scattering, emulsion and development conditions and even mechanical vibrations need to be accounted for. On the other hand, the manufacturer and user of lens systems is interested in measuring the lens performance according to some meaningful criteria after it has been constructed. This article describes two methods for assessing lenses both at their design stage and after construction. A method has been devised which enables images of pictorial objects to be synthesized from data on the lens design and thus enables the lens designer to evaluate realistically the influence on the image of various image-degrading parameters. This system is expected to evolve into an accessory to an electronic computer. Also, an electro-optical bench has been constructed which is capable of presenting simultaneously the frequency response and phase curves of a lens system on a cathode ray oscilloscope, thus allowing measurement of lens performance at various field angles and focal positions in a relatively short time.

## High-Speed Image Synthesizer

A method for convoluting the images of a pictorial test object from the lens design data has been described before[5]. The convolution integral can be written in two dimensions as:

$$h(x,y) = \int_{-\infty}^{+\infty}\int a(x-\eta, y-\xi) f(\eta,\xi)\,d\eta\,d\xi \qquad (1)$$

where the function $a$ is the point spread function of the optical system, $f(\eta,\xi)$ is the object intensity function, and $h(x,y)$ is the image intensity function. One must assume incoherent illumination for the object to allow superposition of the point intensity functions. The spot diagram is a close representation of $a(x,y)$ for optical systems not limited by diffraction and the analysis is valid over regions of the image plane where the aberration function remains constant.

In order to synthesize the optical images of various types of test objects, the intensity distribution function in the point image in the form of a spot diagram (bright spots on a dark background) has been used to illuminate the test object plane (Fig. 1). The convoluted image of the two-dimensional test object is received on an image plane in the form of a shadow of the test object. It is obviously desirable that the test object should not give rise to scattering, therefore test objects on thin emulsions have been used. The distances $d$ and $d'$, and the relative sizes of the object, image and the point spread function simulate the appropriate conjugate relationship and the magnitude of the aberrations under true operating conditions.

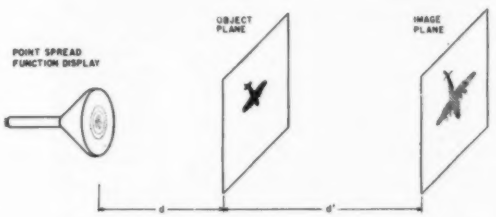


Fig. 1. Optical arrangement of the image synthesizer

The magnification of the test object at the image plane is given by:

$$M_{(\text{object})} = \frac{d + d'}{d} \qquad (2)$$

and the magnification of the point spread function is given by $M_{Sd} = d'/d$. If a periodic line test object is used, the resolution is given by:

$R$ = (test object scale) (spot diagram scale)

$$\frac{M_{Sd}}{1 + M_{Sd}} \qquad (3)$$

This system has been used for measuring image quality in the presence of various types of aberrations using periodic as well as pictorial test objects. Fig. 2*a* shows the theoretical and synthesized intensity gradient in the image of an edge for an $f/2{\cdot}8$, 50 mm. photographic objective at 23° 50′ obliquity. Fig. 2*c* shows the square-wave response for the same lens in the sagittal and tangential directions as measured on the image synthesizer using the calculated spot diagram of the lens system. The pictorial images convoluted by this method have proved to be almost

indistinguishable from actual images produced by the lens built according to the same design. It is also possible to take account of such factors as diffraction, air turbulence and mechanical vibrations by using the point spread function in the presence of these image-degrading parameters. Fig. 2*b* shows the theoretical and experimental edge intensity gradient for a perfect lens as produced on the image synthesizer by approximating the intensity distribution in various rings of the Airy disk with areas of varying spot density.

Having established the performance of the image synthesizing technique and its ability to simulate not only the geometrical aberrations but also other complex phenomena, its application as an accessory to the electronic computer in assisting the lens designer becomes obvious. An approach that seems to offer much promise is the generation of the spot diagram upon the fluorescent screen of a cathode ray tube, the tube screen replacing the photographic plate in the image synthesizer. Thus, the co-ordinates of the spots representing the energy density in the point image can be calculated on an electronic computer, stored digitally either on magnetic tape or paper tape (Fig. 3*a*), and then displayed as successive bright spots on a cathode ray oscilloscope. Basically, the spot pattern is generated automatically by passing the tape through a digital-to-voltage converter using the output voltage from the latter to deflect the electron beam in two orthogonal co-ordinates. In general, it is found that of the order of 300–400 spots render a faithful synthesis of the image. Fig. 3*b* shows the photograph of spot representation of computed data on a cathode ray oscilloscope. As indicated in Fig. 1, this cathode ray oscilloscope is

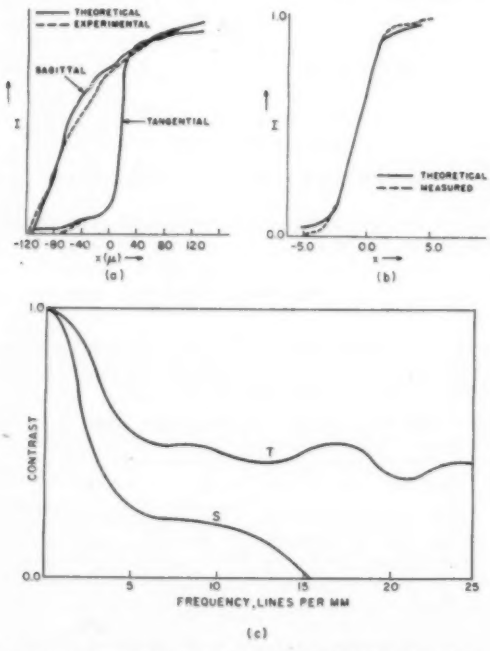


Fig. 2. Image synthesis data: (*a*) theoretical and synthesized edge response of an *F*/2·8, 50 mm. lens at 23° 50′ field angle; (*b*) theoretical and synthesized edge response for a perfect lens, using Airy disk point spread function; (*c*) square wave response for the same lens position (as in Fig. 2*a*) measured on the image synthesizer

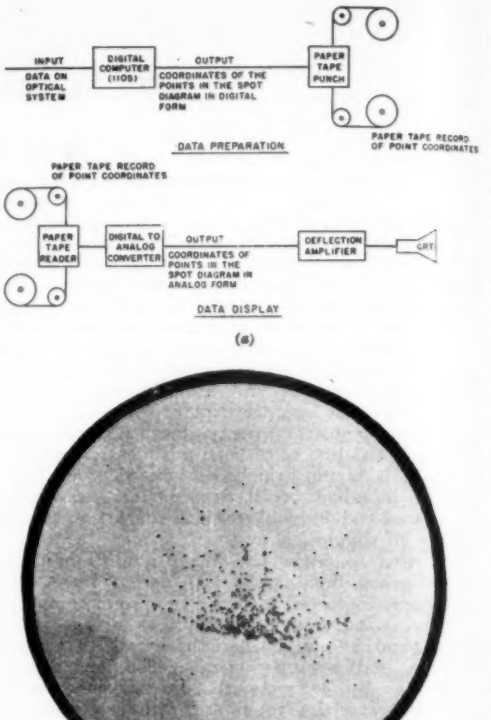


Fig. 3. High-speed image synthesis: (*a*) block diagram of the arrangement for computation of the point spread function and the cathode ray tube display unit; (*b*) a spot diagram displayed on a cathode ray tube

then followed by a simple device consisting of a test object holder and a viewing screen or a photographic plate with variable intermediate distances $d$ and $d'$. This system is thus used for high-speed image synthesis of optical systems while the optical system is still at the design stage.

## Measurement of Frequency Response and Phase Shift

In order to measure the spatial frequency response and the phase shift introduced by optical systems after construction, an electro-optical lens bench has been designed. It is well known[6] that the unidirectional spatial frequency response of an optical system is given by the Fourier transform of its line spread function, that is:

$$F(\omega) = \int_{-\infty}^{+\infty} a(x,y)e^{-2\pi i\omega x}\mathrm{d}x\mathrm{d}y \qquad (4)$$

where $F(\omega)$ is the response for the spatial frequency $(\omega)$ and $a(x,y)$ is the point spread function of the optical system. Here, it is assumed that the point spread function does not vary over the slit-length. Furthermore, for incoherent illumination the simple unidirectional integration of the point spread function yields the line spread function.

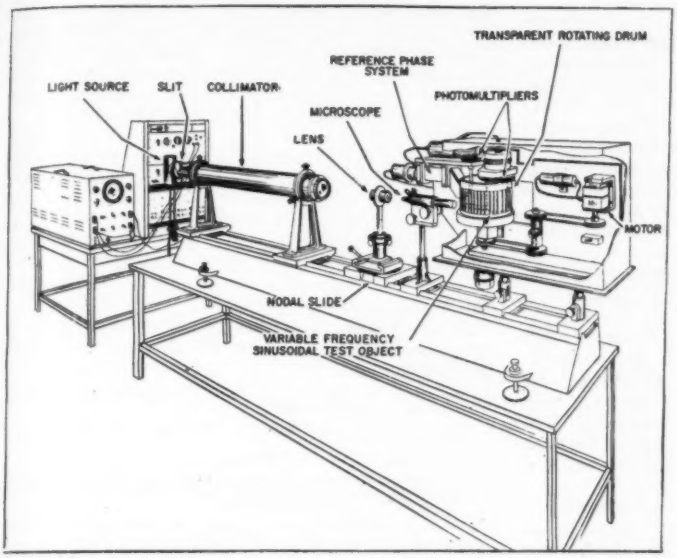


Fig. 4. Illustrating the lens bench for measurement of frequency response and phase of lens system

The principle of this lens bench consists of imaging the line spread function of the lens under test on a rotating glass drum with variable frequency sine wave test objects mounted around it. A photomultiplier receives all the flux, and the contrast in the received signal is a direct measure of the frequency response of the lens. Furthermore, a comparison of this signal with another reference signal yields the phase shift. Both the frequency response and phase shift are presented on a dual beam display scope.

The optical system of the lens bench is illustrated in Fig. 4. A fine slit is placed at the focal plane of a collimator lens, and the lens under test is placed on a nodal slide. The line image formed by the lens under test is imaged at a magnification on the rotating glass drum using a well-corrected microscope objective. The rotating glass drum has mounted around its periphery variable frequency sine wave test objects[7] consisting of 13 frequencies varying in steps of $\sqrt{2}$ and having 24 cycles of each frequency. A stationary photomultiplier placed in the rotating drum receives the signal when different frequencies are presented to the line spread function. The contrast of the received signal, given by the following expression, is a direct measure of the response for that frequency :

$$F(\omega) = \frac{I(\omega)_{\max.} - I(\omega)_{\min.}}{I(\omega)_{\max.} + I(\omega)_{\min.}} \qquad (5)$$

where $I(\omega)_{\max.}$ and $I(\omega)_{\min.}$ are the magnitudes of the signal for a given frequency $\omega$ at the maxima and minima, respectively.

In order to present the frequency response curve on an oscilloscope, the signal from the photomultiplier is amplified linearly, half-wave rectified and applied to an integrator. Using a logarithmic potentiometer geared to the shaft of the rotating glass drum the integrator output is made proportional to the input. This output is gated to a clamp circuit which displays the magnitude of $F(\omega)$ on a cathode ray oscilloscope. Fig. 5*a* shows the frequency response of an $F/6{\cdot}8$, 125 mm. lens system at a 5° field angle with defect of focus, presented on an oscilloscope. The phase shift and spurious resolution are observable at higher frequencies.

The optical system devised to measure the phase change is also shown in Fig. 4. A reference slit is imaged on another portion of the sine wave test object using a highly corrected lens system and the signal is received by another photomultiplier. It is, of course, necessary that the reference slit and the line spread function of the lens under test be in good alignment. The comparison of signals from the two photomultipliers, with the use of appropriate electronics, yields the phase information simultaneously with the frequency response. Fig. 5*b* shows the phase change introduced by the $F/6{\cdot}8$, 125 mm. lens system at a 5° field angle and with a defect of focus, presented on an oscilloscope.

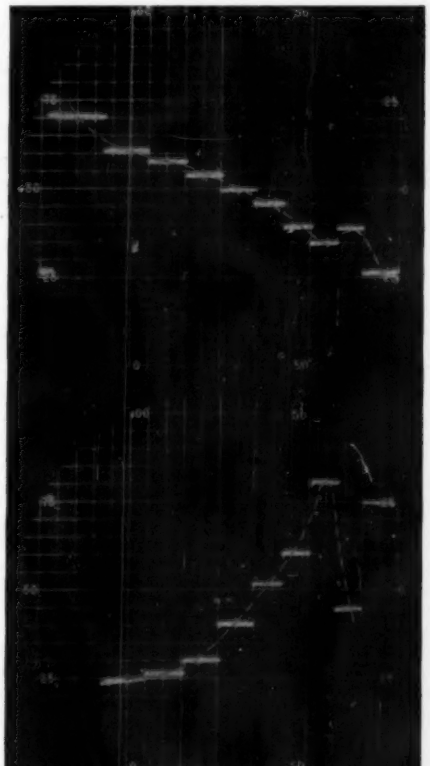


Fig. 5. Cathode ray tube display of frequency response (*a*) and phase (*b*) curves for an $F/6{\cdot}8$, 125 mm. lens system at 5° field angle with defect of focus

## Conclusions

The two techniques described in this article seem to hold considerable promise for optical image assessment both at the lens design stage and after construction, and further work using these methods will be reported elsewhere. The high-speed image synthesizer is useful for evaluating realistically the influence of aberrations, diffraction, atmospheric turbulence and film characteristics, etc., on image quality without having to construct the lens system. Its uniqueness lies in the fact that it is capable of synthesizing images of pictorial test objects as well as conventional test objects. Therefore it can be used to evaluate the influence of psycho-physical effects on recognition and detection. A detailed programme incorporating the image synthesizer with a *Univac* 1105 computer is in progress. As a research tool the image synthesizer is capable of synthesizing images formed by other electro-optical systems such as cathode-ray tube and image intensifiers. Its application to the evaluation of X-ray image-forming systems and high-energy radiographic systems is at present being studied.

An interesting extension of the image synthesizer technique would achieve automatic lens design based on a most meaningful test method. Accordingly, use would be made of a correlation device that compares the synthesized picture with a standard and feeds back an error signal into the computer (Fig. 3*a*). Thus the lens design can be continuously tested on the basis of its 'picture quality', and appropriate changes in the design be made automatically until the correlation function reaches a desired value.

The electro-optical lens bench is particularly valuable for investigating the influence of aberrations and diffraction on spatial frequency response and phase shift of lens systems. Since both curves are presented on the oscilloscope simultaneously, the change introduced at various focal positions and field angles can be studied in much detail. It seems to offer promise as a routine lens bench for lens assembly and evaluation work.

Acknowledgment is due to A. J. Kliore, R. E. Keim and S. H. Cameron for their most valuable assistance.

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# THE ACTION OF NITROUS ACID ON ALIPHATIC AMINES

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ALTHOUGH T. W. J. Taylor in 1928[1] indicated the correct experimental conditions for carrying out the reaction of aliphatic amines with nitrous acid, the essential items in these conditions appear to have been overlooked by other workers who have used other conditions and, not surprisingly, have obtained little or no reaction. As part of a study of the mechanism of deamination by nitrous acid of aliphatic primary amines[2], an investigation of the products formed in the reaction of methylamine with nitrous acid was undertaken; this has not been reported before, because it in turn led to a study of diazotization, which, as the more convenient reaction for detailed kinetic treatment, became for a time the leading sector of attack on the problem of deamination mechanism in general[3].

Taylor described the kinetics of the reaction between methylamine and nitrous acid[1], but so many incorrect statements, most of them in text-books, have been made about the products, that a new account of the matter seems desirable, though it was actually investigated some years ago[4] and in a broader context. There was little doubt that methyl alcohol could be obtained from the reaction of methylamine with nitrous acid, as this had been shown by Linnemann[5], who passed the gas evolved in the decomposition of faintly acidified solutions of methylamine nitrite through water and, on fractionation of this, had obtained the alcohol in good yield (50 per cent). The reaction was next investigated by Whitmore and Thorpe[6], who were apparently unaware of Taylor's fundamental investigation, and, using quite unsatisfactory conditions, these workers were unable to obtain any methyl alcohol. In view of the wide acceptance given to these negative findings, the following observations on the products that are obtainable in the methylamine – nitrous acid reaction are recorded.

The conditions used were those indicated by Taylor's work as being essential for reaction to take place, namely, a solution of the amine containing nitrous acid but—and this is important—no excess of mineral acid. As solutions of nitrous acid are unstable and evolve oxides of nitrogen at concentrations greater than 0·05 *M*, this acid was generated slowly *in situ* during the reaction by gradually adding mineral acid to the amine solution containing dissolved sodium nitrite. In a typical experiment, the methylamine hydrochloride (0·5 mole) was dissolved in water (550 c.c.) together with sodium nitrite (1·5 moles). Sulphuric acid (2 *N*, 0·4–0·6 equiv.) was then run in slowly beneath the surface of the solution. A brisk and steady evolution of gas ensued and the reaction proceeded readily at room temperature until less than 1 per cent of the amine remained. The evolved gas was passed through a container immersed in solid carbon dioxide/acetone mixture and then through a bubbler containing potassium permanganate (to remove oxides of nitrogen from decomposition of the nitrous acid) before being collected in a gas receiver. The products of the reaction in (*a*) the reaction vessel (*b*) the low-temperature trap and (*c*) the gas-holder were then investigated.

Distillation of the pale yellowish-green reaction solution in (*a*) caused the colour to darken to yellowish-brown, which then became opaque-green and much gas was evolved, part of which was carbon dioxide. The colour of the solution then became less intense

and finally pale yellow. A pronounced odour of bitter almonds was observed during the distillation, and this later changed to an ammoniacal odour. These colour changes and odours were shown to be caused by methylnitrolic acid that had been formed in the reaction. Fractionation of the distillate gave, at 64–85°, a two-phase liquid, the upper layer of which was shown to be aqueous methyl alcohol and the lower layer was shown to be mainly nitromethane.

The pale yellow liquid collected in the low-temperature trap (*b*) was shown to consist of a mixture of methyl nitrite (pale yellow, b.p. −18·5°) and methyl chloride (colourless, b.p. −24°). If methylamine hydrobromide was used in the reaction, then methyl bromide (colourless, b.p. 4·6°) was collected in the trap instead of the chloride.

The volume of gas obtained from the reaction at room temperature was slightly greater (3 per cent) than that expected from the reaction :

$$CH_3NH_2 + HNO_2 \rightarrow CH_3OH + N_2 + H_2O \quad (I)$$

The gas was shown to be nitrogen contaminated by a small amount of carbon dioxide.

Table 1. Products formed when Methylamine Hydrochloride (0·5 mole) + Sodium Nitrite (1·5 moles) in Water (550 c.c.) was slowly acidified with 2 *N* Sulphuric Acid (0·4–0·6 Equiv.). Room Temperature

| | Per cent |
|---|---|
| Methyl alcohol | 6–25 |
| Methyl nitrite | 45–35 |
| Methyl chloride | 13 |
| Nitromethane | 6 |
| Methylnitrolic acid | 10–12 |
| Evolved gas (nitrogen + carbon dioxide) | 103 'theoretical' |

These findings may be summarized :

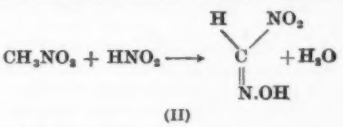
(1) Methylamine readily reacts with solutions containing nitrous acid. *Methyl alcohol* is formed.

(2) *Methyl nitrite* is, however, the major product. This escapes from the reaction vessel owing to its volatility (b.p. −18·5°), and this escape is facilitated by the nitrogen evolved during the reaction. (Identical behaviour is observed in the reaction of ethylamine with nitrous acid and the major product, ethyl nitrite (b.p. 17·4°), condenses in the low-temperature trap.) The methyl nitrite is probably formed by two processes : (*a*) the direct and rapid esterification of the methyl alcohol by the aqueous nitrous acid ; and (*b*) interaction of the methyl carbonium ion at the oxygen end of the ambivalent nitrite ion. The ratio *a*/*b* is not known, but a considerable proportion of the methyl nitrite must be formed via the esterification route since, for a given concentration of sodium nitrite, the amount of methyl nitrite collected in the low-temperature trap was greater the greater the volume of acid added during the reaction. There was a corresponding diminution in the amount of methyl alcohol that could then be isolated from the reaction vessel. This correlation is indicated in Table 1 by the ranges given for the first two items, which should be read together, that is, a low yield of methyl alcohol corresponds to a high yield of methyl nitrite and vice versa.

(3) *Methyl chloride* (*or bromide*) is formed in the presence of chloride (or bromide). It was shown that under the conditions of the reaction, the methyl halide was not formed by esterification of the methyl alcohol by the acid halide. These compounds must therefore be formed as direct reaction products and not arise from secondary reactions.

(4) *Nitromethane* is formed in appreciable amount, and its formation is consistent with the formation of the methyl halides. It was shown by experiment that the nitromethane was not formed by re-arrangement of any of the methyl nitrite, nor was it formed in the direct esterification of the methyl alcohol by the nitrous acid.

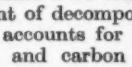
(5) *Methylnitrolic acid* is formed. Experiments confirmed that part of the nitromethane, formed directly in the reaction, had reacted with nitrous acid to give the nitrolic acid in a secondary reaction :



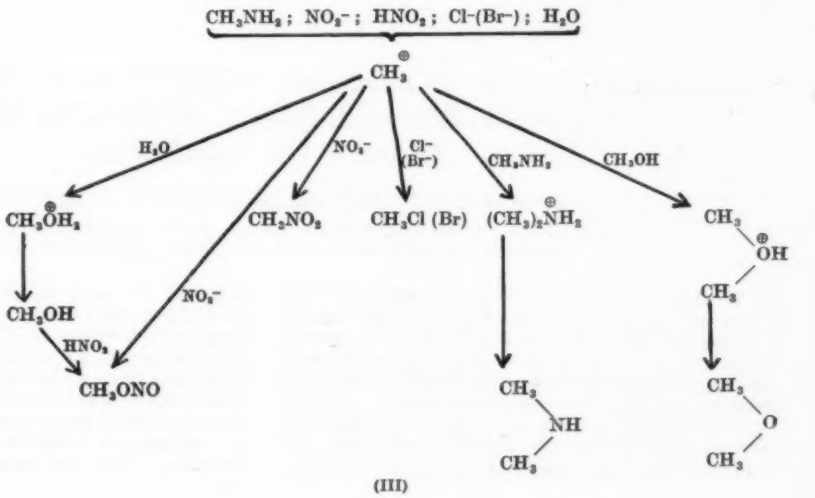

(II)

This acid is unstable and decomposes via well-established reactions and accounts for the colour changes and odours (hydrogen cyanide, ammonia) observed when the reaction residues were heated. It was also shown that the amount of decomposition undergone at room temperature accounts for the slight excess (3 per cent nitrogen and carbon dioxide) of gas collected during the amine–nitrous acid reaction.

The multiplicity of products formed in the above reaction is rationally explained if one assumes that the electron-deficient entity,




is formed—a suggestion originally put forward by Whitmore[7] for this type of reaction. The methylcarbonium ion could interact with a water molecule




(III)

giving $CH_3OH_2^{\oplus}$, which, by loss of a proton to the solvent, would give methyl alcohol. It could unite directly with $Cl^-$ or $Br^-$ giving methyl chloride or bromide respectively. With the ambivalent nitrite ion, a considerable amount of interaction occurs at the *N* atom to give nitromethane. Some attack probably occurs at the O atom to give methyl nitrite directly. Although no secondary amine derivative was isolated from the reaction mixture, such compounds could arise by the $CH_3^{\oplus}$ interacting with some of the unchanged amine, and the formation of secondary amine products has definitely been established by others in this type of reaction[8]. There is also the possibility of formation of ether. This could result from the reaction of the $CH_3^{\oplus}$ with the alcohol formed in the reaction. This is not likely to occur to any appreciable extent in the reaction of methylamine, for the alcohol is swept out of the system as the very volatile nitrite ester. Of course, if an alcohol is used as the solvent for the reaction, it would be expected that the ether would then be the principal product. These reactions may be depicted as in scheme III.

With higher amines yet other reactions are possible for the carbonium ion. Proton loss can result in the formation of olefins and hydrogen, or alkyl groups, from other parts of the ion may migrate to the electron-deficient centre and in so doing create a fresh centre of electron-deficiency at the site vacated. The reactions noted above may then occur at the new centre of electron-deficiency.

The steps leading to the carbonium ion have also been established. Taylor's kinetic findings were confirmed, and the investigations led logically into the aromatic field[3]. Although Piria[9] discovered the 'amine–nitrous acid reaction' by noting the effect of dissolved oxides of nitrogen and assumed that nitrous acid was the effective reagent (thereby setting the pattern of thought for a hundred years) it has now been shown that molecular nitrous acid, as such, is not a participant in the initial interaction with the amine. The squared-term for the nitrous acid in Taylor's kinetic expression has been shown to stand for $N_2O_3$ ($\alpha[HNO_2]^2$), and this as the effective nitrosating entity, originally suggested by Hammett[10], has been placed on adequate experimental foundation together with NOCl, NOBr and NOI. The initial, and rate-determining, step involves an electrophilic attack by $N_2O_3$, NOCl, etc., on the free amine giving a N-nitrosoalkylammonium cation. The inhibiting effect of free mineral acid on the aliphatic amine–nitrous acid reaction is thus readily seen. These amines are so much more basic than their aromatic counterparts that any appreciable protonic concentration will cause the amount of free amine to diminish to vanishing point. Once the N-nitrosation has occurred, the base-weakening effect of the nitroso-group permits ready deprotonation of the nitroso-alkylammonium cation and the primary nitroso-amine then formed undergoes ready tautomeric shift to the diazo-hydroxide. This rapidly ionizes to the diazonium cation which, in the absence of resonance stabilization of aromatic groups, rapidly loses nitrogen giving the electron-deficient carbonium ion. The carbonium ion then undergoes the reactions already noted.

$$R\text{—}\ddot{N}H_2 \xrightarrow[\text{slow}]{NO.X} R.\overset{\oplus}{N}H_2NO^* \longrightarrow R.NH.NO\uparrow \longrightarrow$$

$$R.N{=}N\text{—}OH \longrightarrow R\text{—}\overset{\oplus}{N}_2 + OH^-$$

$$R^{\oplus} + N_2$$

(where $X = NO_2$, Cl, Br, I).

(IV)

* If the original amine was tertiary the nitroso-alkyl ammonium cation could lose an alkyl group giving rise to a N-nitroso-secondary amine.

† If the original amine was a secondary amine the reaction would stop at this stage and the secondary nitrosamine can be isolated.

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# CORRELATION OF BIOLOGICAL ACTIVITY AND THE ELECTRON SPIN RESONANCE SIGNAL STRENGTH FROM GUINEA PIG ADRENALS

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In a previous communication[1] an improved low-temperature technique for the study of free radicals in biological materials was described. This method has now been used to study the relation between electron spin resonance intensities and the level of functional activity in mammalian tissue.

Adrenal glands from large adult male guinea pigs were used. Highly active adrenocortical tissue was produced by daily injections of 5 clinical units of gel-adrenocorticotrophic hormone, followed by a single 5-unit injection of aqueous adrenocorticotrophic hormone 2 hr. before excision of the adrenals. High rates of steroidogenesis and adrenal glutathione turnover[2] are known to occur under these conditions. Hypofunctional glands were produced by suppression of endogenous secretion of adrenocorticotrophic hormone. For this purpose animals were given

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4 mgm. hydrocortisone phosphate by injection daily for five days, followed by a sixth injection of the same amount 2 hr. before being killed. These animals, as well as equal numbers of untreated controls, were killed by decapitation and the adrenals excised as rapidly as possible. Adrenals from 2–3 animals (together with a small amount of isotonic saline to displace trapped air bubbles) were placed in borosilicate glass sample holders of 10 mm. diameter and immersed at once in liquid nitrogen. The weight of tissue plus saline in these samples averaged 1·7 gm. Electron spin resonance measurements were carried out at −180° C. in a conventional $x$-band transmission type spectrometer[3]. The instrument was calibrated before and after each determination, using a secondary standard of coal dispersed in anhydrous dextrose. The resonance absorption had a $g$ value close to that for free electrons ($g = 2{\cdot}0023$). The signal intensity from each sample was adjusted to account for minor changes in cavity $Q$ which occurred from sample to sample. Electron spin resonance runs were also made on sample tubes containing only the frozen saline solution. These measurements showed that essentially none of the resonance absorption obtained from tissue samples could be attributed to the sample tubes or saline solution. As the line-width and shapes for the resonance absorption signals were essentially identical for all samples, the relative electron spin resonance signal strength and thus the relative unpaired electron content could be determined by measuring the peak-to-peak height of the normal electron spin resonance derivative curves. Though no attempt was made to determine the absolute number of paramagnetic species present per gram of sample, the electron spin resonance signal strength obtained for a given amount of tissue was roughly one-fifth of that obtained from freeze-dried rat liver, which contained the order of $10^{-8}$ mole of free electron spin per gram wet tissue[1].

Following electron spin resonance measurement, the non-protein sulphydryl concentration of a number of the samples was determined by a method described elsewhere[2].

Table 1 summarizes the results obtained in five sets of experiments. The intensity of the electron spin resonance signal in the control adrenals varied from 15·1 to 60·1 with a mean value of 31·8. The values of the adrenocorticotrophic hormone-stimulated adrenals ranged from 15·5 to 30·4 with a mean value of 24·2. Statistical analysis shows that this difference has a $t$-value of 2·72 with 12 degrees of freedom, which is significant ($P = 0{\cdot}018$). One may also inspect these results on a non-quantitative basis, that is, that 7 out of 7 deviations (control minus adrenocorticotrophic hormone) are positive. On the basis of the null hypothesis, the probability of such a result occurring by chance is 0·016. The comparison of the electron spin resonance signal strength of the cortisone suppressed adrenals with the control adrenals is less revealing. The values for the cortisone-treated adrenals ranged from 20·9 to 39·4 with a mean value of 32·5. The probability of 4 out of 5 deviations being positive is 0·06. Thus it is reasonable to conclude that the control and adrenocorticotrophic hormone adrenals differ significantly, while no conclusion can be drawn about the suppressed adrenals.

Table 1

| Exp. No. | Control | | ACTH-stimulated | | Cortisone-suppressed | |
|---|---|---|---|---|---|---|
| | ESR signal intensity | SH conc. γ/100 mgm. | ESR signal intensity | SH conc. γ/100 mgm. | ESR signal intensity | SH conc. γ/100 mgm. |
| 1 | 35·7<br>60·1 | | 23·7<br>15·5 | | | |
| 2 | 19·4<br>15·1<br>26·9 | | | | 39·4<br>34·3 | |
| 3 | 37·5<br>31·0<br>31·0 | | 28·1<br>30·4<br>27·2 | | | |
| 4 | 31·6 | 11·5 | 20·1 | 15·7 | 32·7 | 11·8 |
| 5 | 28·5<br>33·0 | 28·6<br>16·6 | 24·3 | 30·8 | 35·1<br>20·9 | 11·6<br>15·8 |
| Mean | 31·8 | | 24·2 | | 32·5 | |

ESR, electron spin resonance; ACTH, adrenocorticotrophic hormone.

It was of interest to compare these changes to the alterations in adrenal sulphydryl concentration and turnover at the various levels of adrenocortical activity. It has been shown in rats[3] that acute stimulation of the adrenal cortex causes a marked, transient increase in sulphydryl concentration and turnover. Inactivation of the adrenals (by hypophysectomy) causes no change in the sulphydryl concentration but some diminution of the turnover rate. Since some stable organic free radicals, as in the case of α,α diphenyl β-picrylhydrazyl[5], may be expected to react with available sulphydryl groups, one may well wonder whether or not the decrease in free radicals (and thus the electron spin resonance signal level) in stimulated adrenal tissue is not correlated with the known rise in glutathione. For this reason, adrenal non-protein sulphydryl determinations were carried out in experiments 4 and 5. Unfortunately, the individual variations in SH concentration were large, greatly exceeding those observed in homogeneous rat populations. This variation (and possibly that in electron spin resonance signal intensity as well) may be related to the fact that the largest and therefore oldest animals available were used, to provide the maximum amount of adrenal tissue. This variance precluded the possibility of demonstrating SH changes such as are known to occur in rat adrenals.

There are many possible interpretations of these data other than a potential relationship of the electron spin resonance changes to sulphydryl alterations. Other reducing agents such as ascorbic acid could act in the same manner as SH groups. However, under the conditions of the experiment the tissue concentration of ascorbic acid is sharply reduced rather than increased as is glutathione. It may be noted that our electron spin resonance findings are at variance with those of Commoner *et al.*[4]. However, these authors based their conclusions on a comparison of different tissues rather than on a study of the same tissue at different levels of activity, which we believe would be a far more valid criterion. Moreover, the high levels of electron spin resonance signal intensity found by Commoner in lyophilized tissues may well have been due to sorbed molecular oxygen[6]. The possibility that our tissue electron spin resonance signals were in part due to paramagnetic ions is recognized, and much work needs to be done to determine to what extent such ions contribute to the observed electron spin resonance signal. However, the work of Heggen and Strock[7] shows that for rat liver tissue the content of paramagnetic ions having a $g$ value close to 2·00 can account only in part for the electron spin resonance signal intensities observed[1].

Whether or not the paramagnetic ion content of guinea pig adrenal tissue is high enough to contribute to the electron spin resonance signals observed is at present under investigation.

It is also important to consider whether the electron spin resonance values obtained can be related to concentrations of free radical in a simple manner or whether the lifetime of the free radicals must be taken into account. The temperatures at which measurements were carried out (− 180° C.) tended to reduce this problem; moreover, our previous work on aged rat liver[1] indicates that at the temperature of observation the free radicals present are relatively stable.

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# THEORIES OF SHAPE DISCRIMINATION IN *OCTOPUS*

SUTHERLAND, in a recent article[1], offers an evaluation of my theory of the relation of the plexiform zone in the octopus to its shape discriminatory capacity[2]. A critique is made both on general grounds of plausibility and in relation to specific points of experimental evidence. Dr. Sutherland seems to misunderstand my theory, for his article contains important errors. There are six main objections which will be dealt with in turn.

(1) It can be seen from Cajal's neurohistological work that the retinal fibres of the octopus terminate in the plexiform zone, which they penetrate at right angles. This plexiform zone is seen to consist of a large number of fibres lying in many layers parallel to each other. Each fibre runs only a certain distance among this plexiform zone and sends a process out of this zone deeper into the optic lobes. Beyond these neurohistological observations made by Cajal, I further proposed that we make two main suppositions. The first was that each fibre in the plexiform zone sent a message out only when two or more simultaneously active retinal fibres cross it. The second was that the fibres in the plexiform zone ran in a vertical direction in relation to the visual field of the octopus. Given only these simple suppositions, it was shown that the observed neurohistological arrangement would convert vertical distances between points into amounts of activity leaving the plexiform zone. The smaller the distance between two points, the larger the amount of activity. It was made explicit that no precise mathematical relation between distance and output was postulated. "It should also be stated that the present system has been left quantitatively flexible. It has been assumed, for example, that the vertical distance between two points leads to an output which is the reciprocal of this distance. There is no reason for supposing that the conversion is precisely this. The theory only has to assume that the conversion is something like this and then not over the whole range". The conversion will depend, among other things, on the distribution of fibre-lengths in the plexiform zone. Further, it was assumed that the output from all such vertical arrangements was summed to produce a message for each visual pattern presented to the octopus.

Sutherland, in his review, fails to mention the neural mechanism postulated. He says: "He suggests that octopuses count distances between contours in the vertical direction at all points along the horizontal axis. The count is made in such a way that the reciprocal of the distance between contours is taken". Having thus omitted my qualifications, he then points out that as a result the number infinity will be obtained from shapes containing intersections of lines away from the vertical or horizontal axis. Apart from such considerations that, within the neural system described, counts of infinity are impossible, that infinity can be arbitrarily assigned some low value in terms of frequency of impulses, it was clearly stipulated in one of the two accessory assumptions made by me, that "excitations on the same vertical arrangement inhibit each other over a small distance".

(2) On the mechanism put forward, all shapes are transformed into a point on a dimension of amount of neural activity. Sutherland writes: "On general grounds this theory is rather implausible, since it is possible to find a horizontal or vertical rectangle which is on the same point on this dimension as any other shape however complex: it would be difficult to test this prediction, but it seems most unlikely to be correct". First of all, the deduction which Sutherland draws is incorrect. This is simply demonstrated by imagining the longest and narrowest horizontal rectangle the octopus can see. A pattern not equivalent to this can obviously be constructed by placing another such horizontal rectangle some distance above it. Such a procedure can be repeated until we have a whole field of horizontal stripes, which evidently cannot be equivalent to any horizontal rectangle. Conversely, there will be complex shapes which are not equivalent to any horizontal rectangle but to some field of stripes. What is of more interest is that he himself suggests a principle of classification for the octopus at the end of his article and in other publications on which precisely analogous equivalences can be constructed. He suggests that an analysing mechanism in the octopus is present which computes the total contour of a shape relative to its area or to the square root of its area.

Further in support of his suggestion, he reports an experiment in which there was good transfer from a butterfly shape to an elongated rectangle. Though these considerations are not claimed in support of

my theory, it is difficult to see why Sutherland regards my theory as "rather implausible" on grounds which apply to his suggestions and which, as he himself recognizes elsewhere, his own experiments tend to refute.

(3) A further criticism of my theory concerns the result of transfer tests to the same shape of different sizes. On my theory, transfer to the same shapes of different size would be predicted to varying degrees depending on both the shapes used in the original training. If we assume some kind of reciprocal relation between distance and amount of excitation on the vertical axis, then doubling the distance of two points will decrease the excitation emerging from the plexiform zone. On the other hand, if we enlarge a shape, we not only increase the distance between the contours in the vertical axis, but also increase the number of pairs of points on the horizontal axis. So, when we increase the distance vertically, we also increase it horizontally, so that the total amount of excitation for certain classes of shapes, such as squares, when scaled up or down tends to remain the same. It follows, as I further wrote: "Transfer from one shape to another will depend on two factors: (*a*) the shape used; and (*b*) the other member of the pair from which the octopus has learnt to make the discrimination. . . . As regards the first point, it will be readily seen that, if we take a V shape lying on its side and a scale enlargement of it, the scale enlargement will produce a greater output. The small V shape is a part of the larger V shape. . . ".

"This brings me to the second point. If the total amount of output from the shape to be discriminated from the other member of the pair was larger, then the increase in output due to the enlargement of this shape will not destroy the discrimination, because the effective distance along the continuum is increased. . . . There may actually be an improvement if the other parameters which the octopus derives from the stimulus also increase the distance between discriminanda"[2]. Sutherland, however, states: "Thus the theory predicts good transfer to different sized rectangles, but poor transfer to different sized triangles. These predictions are not confirmed: there is diminished transfer to all figures including vertical and horizontal rectangles when the area is reduced by a quarter. There is usually better transfer to larger figures than to smaller, though even this transfer is sometimes less than complete. The results of transfer tests to different sized figures thus constitute a direct refutation of one of the most interesting predictions made by *B* (Deutsch's theory)".

I am sorry that Sutherland has missed the point that overall trends in efficiency of transfer to different sizes are of little theoretical interest given his experimental situation. It is the comparative efficiency for a given shape, when it is being discriminated from a certain other, that is of interest. Here there are indications of variation, though the results are unfortunately confounded through a process of averaging. For example, Sutherland[4] reports that with certain pairs of shapes the transfer to shapes of 4/9 the area is better than to the originals. He also ignores similar interesting discrepancies from his generalization to be found in another of his papers[5]. It should be clear that, for some reason, Sutherland ignores the stipulation concerning the other member of the pair of shapes being discriminated which was clearly made. In fact, so far from making the transfer to different-sized triangles worse, I actually quoted an example from Sutherland's results in support of my theory, in which there was an improvement in accuracy of discrimination between a triangle and a square when the triangle was made larger.

I was well aware of the data on worse transfer to smaller shapes and comparatively better transfer to larger shapes which Sutherland quotes and which, according to him, "cannot be directly explained on any current theory", and for which he postulates some effect of noise in the neural analysing mechanisms. These data I carefully avoided discussing to spare Sutherland the embarrassment of pointing out that this may be explained as a simple artefact of his training situation, in which the octopus swims up to the shapes presented, thus exposing itself to progressively larger projections of the shape before it is finally rewarded or punished; however, no analogous shrinking of the shape to a smaller size than that presented is allowed to occur. We cannot, therefore, regard it as surprising that transfer to larger shapes is better than that to smaller.

In view of this, I was careful to quote only evidence which compares the effectiveness of transfer for different shapes. Sutherland has not denied the validity of these data.

(4, 5, 6) Three of Sutherland's further criticisms are again due to a failure to take note of one of the two accessory assumptions made by me:

"Before proceeding, I should make clear that for the purposes of prediction two accessory assumptions must be made . . . (2) that the octopus can also discriminate relative vertical positions of the output converted in the above way. This second appears to be a residual factor left when we have explained the rest of Sutherland's results". Though this is certainly not an explanation, it clearly limits the scope of my theory. In spite of this, the theory is criticized as if no such limitation had been made (Sutherland's points under his headings 2, 4 and 10). This failure is especially outstanding in the case of 10. I state: "It is found that the octopus can discriminate some up–down mirror images. This would be covered by assumption 2". Sutherland, however, says: "*B* [my theory] cannot account for any discrimination between mirror image shapes of this sort . . .". Such criticisms are all the more remarkable as in the very same paragraph he imports special assumptions into his own theory to explain these findings, " . . . behaviour is more accurately controlled by differences in the horizontal projection (on which up–down mirror images differ) than by differences in the vertical projection". He then goes on to state that using this principle of more accurate analysis on the horizontal projection to predict, it would be the case that "horizontal rectangles of different lengths will be more readily discriminable than vertical rectangles of different lengths (this follows because horizontal extent is more accurately analysed than vertical extent). This prediction was strikingly confirmed". If it were, then it disproves the theory, or shows it to be nonsense. If "behaviour is more accurately controlled by differences in the horizontal projection (on which up–down mirror images differ)" then vertical rectangles ought to be more readily discriminated, as they will differ on the same projection as up–down mirror images. The same confusion between vertical and horizontal (which Sutherland has shown the octopus can discriminate) is shown

when Young's[6] neuroanatomical data on the dendritic fields of pick-up fibres from the input to the optic lobe are quoted by Sutherland in support of his own theory. "Moreover, there appear to be more fields orientated in the horizontal than in the vertical axis: this would be expected on the theory if the function of these cells was to compute horizontal and vertical extents". Young[6], however, states about these structures: "Measurements on Cajal preparations show the greatest number and total length of dendrite to be in the vertical direction". Such a statement is amply borne out by the numerical analysis given by Young in Table 1 of his paper.

Young's work is fully consistent with my own theory, and his new findings enable the mechanism suggested in the theory to be applied to explain data which previously were outside its scope (for example, Sutherland[4]). It is hoped to deal with this in another publication.

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In a recent article on shape discrimination in the octopus[1], I reviewed the behavioural evidence and its bearing on three theories which have been proposed. One of these theories was that put forward by me[2], a second was a modified form of this theory suggested by Deutsch[3].

In the foregoing communication, Deutsch attempts to rebut four of the criticisms made of his own theory in the light of the evidence, and also criticizes my theory at two points. Both the experimental evidence and its bearing on theory are now rather complex, and Deutsch appears to have misunderstood some of my original article: because of the complexity of the evidence and the brevity with which it was summarized, it is possible that parts of this article were not clear to others besides Deutsch, and the present communication will attempt to expand those points at which Deutsch's article reveals that there is a possibility of misunderstanding. His points will be dealt with in turn using the same numbering as in his communication above, and an attempt made to clarify dispassionately the questions at issue.

(1) One crux in Deutsch's theory is to specify what happens when the contours of a figure approach one another in such a way that the vertical distance between contours approaches continuously to zero. Fig. 1 shows four shapes, in three of which this occurs at the corners marked with a vertical line. Deutsch's mechanism analyses shapes in terms of the closeness in the vertical direction of their contours: when the vertical distance between contours falls below a certain distance ($D$) no count is taken. The vertical lines in the corners of shapes in Fig. 1 represent an example of what this distance might be. I did not fail to recognize that such a distance ($D$) could be specified in my article[1]—indeed, in my summary of Deutsch's theory I wrote that "to prevent obtaining infinity from such shapes, it would be necessary to specify some small vertical distance between contours within which no count is taken". The point at issue is that Deutsch has failed to specify what this distance is, and until it is specified it is impossible to make predictions on his theory about the discriminability of shapes with contours approaching one another in this way. This of course includes the vast majority of shapes in the octopus's normal environment, so that without specifying this distance the theory has little predictive value. However, once this distance is specified the theory would make different predictions from my own at some points. The question arises why Deutsch has failed to make his theory more precise by specifying a distance, and the answer would appear to be that whatever distance is selected predictions about some pairs of shapes are yielded which the experimental evidence already in existence shows to be false: the points at which false predictions will occur will of course vary with the actual distance specified. A second problem which Deutsch has not considered is that it is difficult to know whether to specify the distance ($D$) in terms of the physical size of the shape, or in terms of retinal angle. We find ourselves in a dilemma: the former alternative would require an elaborate neural mechanism to achieve constancy of visual size independent of how far from the eye a shape is placed operating before the count of vertical extents is taken. The latter alternative would mean that the count yielded by a shape would vary with its distance from the eye. Thus the question of what the vertical distance ($D$) is within which no count is taken is critical for Deutsch's theory since, until it is specified, the theory cannot make predictions about most shapes, and there are serious difficulties in specifying such a distance.

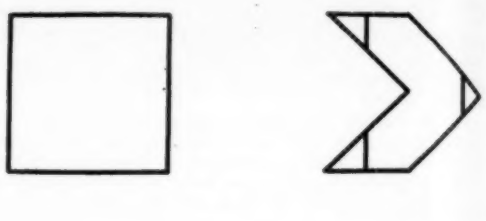

Fig. 1

(2) Deutsch's claim that it would be possible to find a pattern of stripes not equivalent to a horizontal rectangle on his theory is irrelevant to the argument. My claim was that it would be possible to match any shape (not any pattern) by a vertical or horizontal rectangle of appropriate dimensions. How one evaluates the plausibility and biological utility of a mechanism which makes confusions of this sort is a matter for individual judgment. The point at issue is that Deutsch's mechanism confuses every closed shape with the appropriate horizontal or vertical

rectangle: the mechanism I proposed only confuses certain shapes, and has led to tests for whether or not these confusions actually occur.

(3) The predictions Deutsch should make about transfer to different-sized shapes can be stated succinctly as follows. Let us suppose that an animal has learned to discriminate between two shapes *A* and *B*, where *A* occupies a higher position on the dimension under analysis according to Deutsch than the position occupied by *B*. For some shapes (for example, horizontal and vertical rectangles, a square), changing their size does not alter their position on this dimension; for other shapes (for example, triangles, cf. Fig. 2 (*b*) in ref. 1), if the shape is enlarged, its position on the dimension is increased; if it is reduced in size, its position is decreased. We can now make the following predictions: (i) For all shapes of the former sort, transfer should be perfect to both smaller and larger shapes. This applies to both *A*- and *B*-type shapes, since neither changes its position on the dimension. This prediction has been shown to be wrong with no fewer than six pairs of shapes (horizontal and vertical rectangles[4], square and vertical rectangle[5], square and horizontal rectangle[6] pairs *jk* and *lm* in Fig. 1 of ref. 1, square and cross). In all these cases transfer was found to be better to larger shapes than to smaller. The following predictions can be made of shapes which do change their position on the dimension when their size is changed. (ii) If shape *A* is enlarged transfer will be complete since it will be pushed further away from shape *B* along the dimension. It is even possible (but unlikely, cf. the experimental evidence in ref. 6) that performance may now be better than on the training shapes used. (iii) If shape *A* is made smaller, transfer will be imperfect since it is now closer to shape *B* on the dimension. (iv) If shape *B* is enlarged, transfer will be incomplete since it now lies nearer *A*. (v) If shape *B* is reduced in size, transfer will be complete (or better than complete) since it now lies further away from shape *A* on the dimension under analysis. Predictions (ii) and (iii) are of little interest since they are covered by the generalization that better transfer results with larger figures than with smaller. Nevertheless, Deutsch rests his whole case on a prediction of type (ii). From some 40 examples of transfer to shapes of different sizes to be found in my experimental papers, Deutsch selects one result and claims it supports his theory. In this experiment[7] I had trained four animals to discriminate between a triangle (shape *A*) and a diamond (shape *B*) and four to discriminate between a triangle (*A*) and a square (*B*). When an enlarged triangle was presented transfer was better than complete. The very same experiment from which Deutsch takes this result provides data on transfer tests to three other shapes of different sizes, every single one of which gives a result contrary to the predictions which would be made on Deutsch's hypothesis. Thus we would expect worse transfer to a small triangle than to a small square, since reducing the size of the triangle (shape *A*) brings the shape nearer to the square on the dimension under analysis (prediction iii). Yet transfer to the small triangle and to the small square was the same and was complete. Moreover, when we increase the size of a diamond we bring the figure nearer to a triangle on this dimension (prediction iv), yet performance was as good as with the original diamond. Finally, if we reduce the size of the diamond, performance should improve since it moves away from the position of the triangle (prediction v). Performance did not improve: it was the same as with the small triangle. Thus even in the one experiment which Deutsch cites as providing evidence favourable to his hypothesis on transfer, there are three cases (not mentioned by Deutsch) where the predictions his theory makes were found to be incorrect, and one (cited by Deutsch) where the prediction was right. It is about this question that he now writes, "Sutherland has not denied the validity of these data".

In his discussion of size transfer, Deutsch further writes that the better transfer to larger shapes than to smaller "may be explained as a simple artefact of his [Sutherland's] training situation". This might well have been true, were it not for two facts: (*a*) Better transfer to larger shapes than to smaller has been found to occur in all species tested, irrespective of the training situation used. (*b*) In a recent experiment (to be published), J. Z. Young has shown that better transfer to larger shapes than to smaller occurs quite independently of octopuses' previous experience with shapes of different retinal sizes.

(4) Deutsch in his original article claimed it would be possible to put a further mechanism into his theory which would account for the discrimination of up–down mirror images. In the foregoing article he says "this is certainly not an explanation": it was for this reason that I did not discuss his unspecified further mechanism. It should be noted, however, that even if a count of contour position in the vertical plane is kept, this will still not explain discrimination of left–right mirror image shapes: my original claim that Deutsch's theory "cannot account for any discrimination of mirror-image shapes of this sort" (that is, left-right) is therefore correct. It is not clear why Deutsch thinks his further mechanism is relevant to points (2) and (4) in my original article[1]. He appears to be claiming that at all points where his theory makes incorrect predictions it would be possible to propose some other mechanism which would make correct predictions: this claim is irrefutable.

(5) The allegation that the greater discriminability of horizontal rectangles of different lengths than of vertical rectangles of different lengths disproves my original theory is surprising. This experiment was performed in order to test a prediction made by my own theory. Fig. 2 should help to make clear on what the prediction was based. The vertical and horizontal projections respectively represent the amount of each shape in the vertical plane at each point on the horizontal axis, and the amount of each shape in the horizontal plane at each point on the vertical axis. It should be noted that the horizontal projections have been rotated clockwise through 90°. In all my papers on this subject, it has been stated that it was the heights of these projections which are analysed, not their breadths. It is clear from Fig. 2 that left–right mirror images (pair *b*) differ only in their vertical projections, whereas up–down mirror images (pair *a*) differ only in their horizontal projections. Up–down mirror images are better discriminated by octopuses than left–right. In terms of my theory this can only mean that when discrimination is based on an analysis of the horizontal projections performance is more accurate than when it is based on an analysis of the vertical projections. This enables us to construct a further test for the theory: two horizontal rectangles of different lengths differ in the height of their horizontal projections,

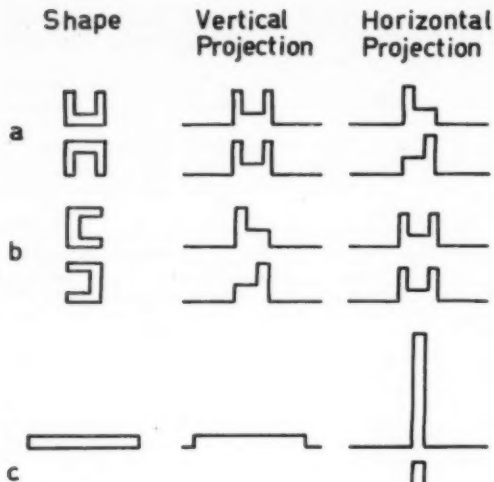


Fig. 2

two vertical rectangles differ in the height of their vertical projections (cf. Fig. 2, pairs *c* and *d*). The theory must predict that the horizontal rectangles will be better discriminated than the vertical. This prediction was confirmed. In my original article, I said it was "*strikingly*" confirmed; the difference in performance of animals trained on rectangles in different orientations was very large and was significant at better than the 0·00001 level of confidence[6]; also this was a new and (to common sense) unexpected discovery about the octopus, which would not have been found out if the theory had not been manipulated to yield predictions.

(6) Deutsch's final point appears to involve certain misconceptions about neuroanatomy and in particular about Young's recent findings[8]. From a functional point of view, what is likely to be important is not simply the total length of dendrite running in the direction corresponding to a given optical axis, but the orientation of dendritic pick-up fields. Young has tentatively interpreted his own findings to mean that there are more dendritic fields orientated in a plane corresponding to the visual horizontal than in any other plane. This might produce better discriminability of horizontal extents than of vertical, and is therefore in line both with the behavioural evidence and with my speculative interpretations. To consider only the direction in which fibres are running, which is what Deutsch appears to be doing, is like trying to draw conclusions about a radio set by looking only at the directions in which wires go without considering how they are linked up. On Deutsch's own theory we would expect to find better discriminability of vertical than of horizontal distances, and correspondingly more vertically orientated pick-up fields than horizontally orientated; thus the theory appears to be at variance both with the existing neuroanatomical and behavioural evidence.

In conclusion, it may be worth attempting to draw some lessons of a more general kind from this controversy. From behavioural data alone it is not possible to specify the exact neurophysiological mechanisms at work and it would be presumptuous for a psychologist to attempt to do so. Such specification must await the results of detailed neurophysiological and neuroanatomical studies: in the existing state of such studies it is only too easy for the psychologist to produce howlers in his attempts to interpret them. All the psychologist can hope to do is to specify the general lines along which data are processed in the system. I have attempted to work out by systematic experiment some of the ways in which visual data are processed by the octopus: any neurophysiological hypotheses I have proposed have been put forward only to give concrete instances of the sort of thing that may be happening, and as a help in framing hypotheses which may be tested at a behavioural level. Deutsch does not challenge the outlines of the data-processing system, that is, that there is an analysis of shape along the $x$ and $y$ co-ordinates with a greater accuracy of analysis on the horizontal co-ordinate. The point of neurophysiological speculation at this stage is only that thinking in concrete terms may help to produce hypotheses which can be tested by behavioural experiments: it is in fact heuristicly valuable and in the case of the octopus has helped me in the assembly of systematic data on this species' capacity for shape recognition, and in the discovery of some surprising facts. These facts may help in the interpretation of neurophysiological and neuroanatomical data when more complete data of this sort become available. Unfortunately, Deutsch's theory has not led to the discovery of any facts, nor has it yet made any new and correct predictions; if further specifications could be added, then it too might become valuable as a research tool. The body of experimental data on shape recognition in the octopus, collected by Young, Boycott, Muntz and Sutherland, is now fairly extensive; for almost any theory which could be proposed it would be possible to select a few facts out of many, quote them out of their experimental context and claim that these facts fit the theory. The progress of a science is not favoured, however, if in doing this we take no note of the facts which do not fit the theory: these may be the most important points at which to start further work.

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# LETTERS TO THE EDITORS

## PHYSICS

### Pressure Dependence of Resistivity of Indium Antimonide to 70,000 Atmospheres

THE pressure dependence of the resistivity of indium antimonide has been measured by Keyes[1] up to 12,000 atmospheres. We have extended the range to 70,000 atmospheres. In addition to the type of change found by Keyes we have observed a resistance change on melting when the temperature was considerably below the zero pressure melting-point of 796° K.

The measurements were made in a tetrahedral apparatus constructed at the National Physical Laboratory following a design of the National Bureau of Standards[2]. This allows the use of a standard hydraulic press. In our apparatus the pyrophyllite tetrahedron had a side of $\frac{3}{4}$ in. and electrical connexions were made by the techniques described by Hall[3]. Cooling coils allowed the temperature to be lowered to 120° K. Pressure-versus-load calibration was made by measuring resistance changes in bismuth, thallium and barium specimens and using Bridgman's electrical data[4].

Fig. 1 shows typical behaviour of single-crystal specimens of indium antimonide at two temperatures. Initially, the resistance increases with pressure as found by Keyes, who showed that this effect comes mainly from a widening of the energy gap. In our room-temperature experiments, the resistance dropped sharply at a pressure of 30,000 atmospheres. This is attributed to melting, with a transition from semi-

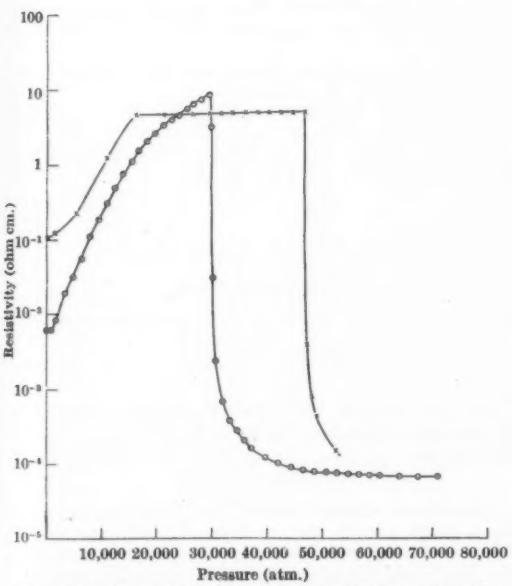


Fig. 1. Behaviour of single-crystal specimens of indium antimonide at two temperatures. n type ~ 4 × 10¹⁴ electrons/c.c. Specimen size, 1½ mm. × 1½ mm. × 3 mm. ○, 293° K.; ×, 184° K.

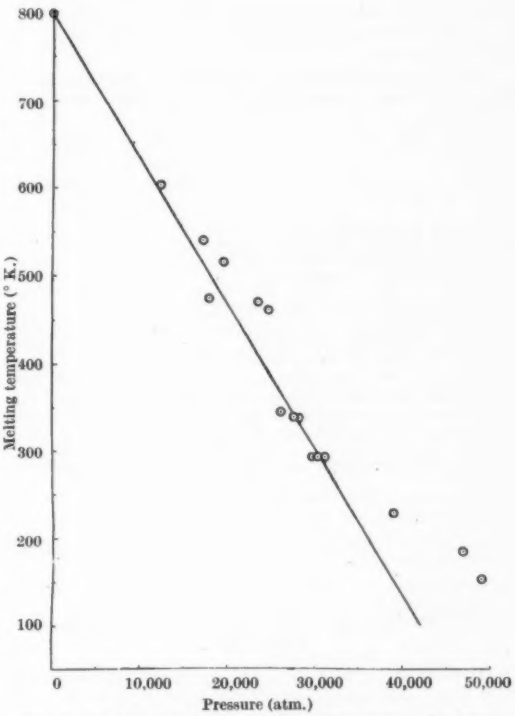


Fig. 2. Effect of pressure on the melting point of indium antimonide

conduction in the crystal to metallic conduction in the liquid phase. In support of this, the ultimate resistivity reached here is close to the value obtained by Busch[5] for liquid indium antimonide at zero pressure. The small pressure dependence of the resistivity in the liquid phase is also consistent with the metallic behaviour demonstrated by Busch.

Fig. 2 shows the melting point, as measured by the sharp fall in resistance, plotted as a function of pressure. It shows a decrease with increasing pressure which, qualitatively, is consistent with the known contraction in volume on melting shown by this compound. The decrease varies linearly with pressure to about 30,000 atmospheres, but significantly departs from this behaviour at higher pressures. By inserting a value of the slope of our melting curve at zero pressure in the Clausius–Clapeyron equation with a known value[6] of the volume contraction on melting ($\Delta v/v_{solid} = 0{\cdot}13$) a value for the latent heat of fusion can be found. This value of 27 cal./gm. does not agree with an experimentally determined value[7] of 47·2 cal./gm. The disagreement between these values might arise from the presence of complex phases in the liquid near the melting point[8]. In our experiments results are lacking below 10,000 atmospheres because the pyrophyllite gasket technique is not reliable.

It is interesting to compare the corresponding work on the melting of germanium by Hall[9]. In this he finds a variation of melting point with pressure which is substantially linear over the range 0–180,000 atmospheres. When his value of the slope of the melting curve is used to calculate the latent heat of fusion, using a measured value[10] of the volume change, a value of 84 cal./gm. is found which is in fair agreement with the experimentally determined value of 110 cal./gm.[11].

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## Diffusion of Cadmium into Gallium Arsenide

Diffusion of cadmium-115 into gallium arsenide has been examined by a method identical to that described by us[1] in the case of zinc-65. The cadmium was diffused from a saturated vapour into a carefully prepared specimen of gallium arsenide approximately 1 cm. × 0·4 cm. × 0·2 cm. contained in a quartz tube 2 cm.³ in volume. After diffusion auto-radiographs of the specimen were taken to check the uniformity of activity across the surface and the diffusion profile was obtained by sectioning as described in the reference.

Fig. 1 shows typical diffusion profiles after diffusion for 40 hr. at 1,000° C. with the cadmium source held at 750° C.

The initial decrease in concentration from $2 \times 10^{19}$ cm.$^{-3}$ at the surface is very rapid. Fitting this part of the curve to a complementary error function, an approximate diffusion coefficient, $D$, of $3 \times 10^{-12}$ cm.$^2$ sec.$^{-1}$ can be obtained. The concentration falls to a minimum, which is sometimes below the limit of detectability, but rises again to a maximum followed by a much more gradual decrease. Twelve different specimens have been examined and all have shown the same qualitative results. The half-life of the deeply penetrating activity has been measured and found to be the same as that of the irradiated cadmium, thus ruling out the possibility that the effect is due to an impurity in the cadmium. Although the steeply falling portion of the profile is reproducible, the concentration at the subsequent maximum has varied between $4 \times 10^{18}$ cm.$^{-3}$ and $\sim 10^{16}$ cm.$^{-3}$ in a manner which is at present unaccountable.

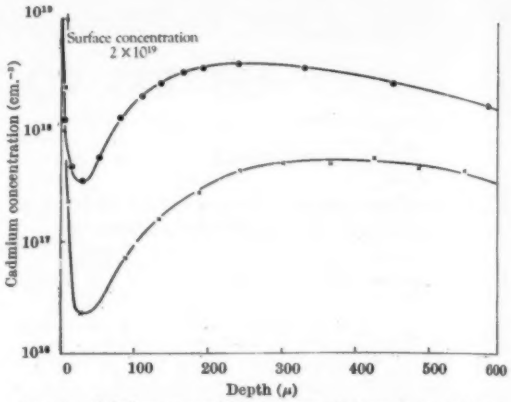


Fig. 1. Cadmium concentration versus distance from surface. Diffusion temperature, 1,000° C.; diffusion time, 40 hr.; cadmium source temperature, 750° C.

Goldstein[2] has also examined the diffusion of cadmium into gallium arsenide and fits his results to simple complementary error functions. The value of $D$ which he obtains for 1,000° C. is somewhat higher than that which we obtain from the steeply falling portion of our curves. He does not report any anomalies in his results such as we have found. However, it should be noted that his conditions of diffusion are somewhat different from ours, and in particular he has chosen to carry out diffusion in the presence of an arsenic atmosphere.

In an attempt to explain this behaviour experiments have been performed using :

(1) crystals of different conductivity type ;
(2) crystals orientated so that diffusion along [111], [$\bar{1}\bar{1}\bar{1}$], [110] or [100] directions was examined ;
(3) crystals strained to produce a large concentration of dislocations.

No correlation has been found between these crystal properties and the characteristics of the diffusion profile.

Further experiments to elucidate the mechanism of this diffusion are in progress.

We wish to thank the Admiralty for permission to publish this communication, Mr. W. R. Harding for supplying the gallium arsenide and Mr. N. Fleet for assistance with the experiments.

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## Fine Structure of the Nuclear Magnetic Resonance Spectra of Solids: Chemical Shift Structure of the Spectrum of Phosphorus Pentachloride

The static dipolar interaction between the nuclei in a solid causes its nuclear magnetic resonance spectrum to be much broader than that of a liquid. In the liquid state the isotropic re-orientation and diffusion of the molecules average their nuclear dipolar interaction almost to zero, often revealing a

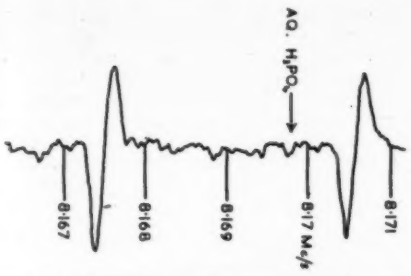


Fig. 1. Phosphorus-31 magnetic resonance spectrum of polycrystalline phosphorus pentachloride rotated at high speed. The resonance frequency of the reference compound (85 per cent aqueous phosphoric acid) is also indicated; this frequency was determined from recordings taken immediately beforehand and afterwards

fine structure originating from the different chemical shifts of the nuclei, and from their indirect spin–spin interactions. In solids this fine structure is obscured by the stronger dipolar interactions. As we have shown previously[1–3], the dipolar broadening may nevertheless be removed in solids also, the necessary averaging being achieved by high-speed rotation about an axis inclined at an angle 54° 44′ to the direction of the applied field. When the rotation-rate is comparable with the static line-width, the narrowed central line is resolved from the satellite lines which appear on either side of it at integral multiples of the rotation frequency. Thus, for example, rotation of solid sodium chloride at a rate of 800 c./s. gives a resolved sodium-23 spectrum consisting of a central line and three pairs of satellites[2]. At a rotation-rate of 1,600 c./s. the central line and only one pair of weak well-resolved satellites are observed, while at 2,500 c./s. only the narrow central line is visible.

High-speed rotation at the angle 54° 44′ thus opens up the possibility of observing fine structure in solid specimens, and may therefore be useful in studying insoluble compounds. There is in any event interest in comparing the fine structure of spectra for the same compound in both the solid and the liquid states.

A first example of the application of this method is provided by polycrystalline phosphorus pentachloride, which gave the phosphorus-31 resonance spectrum shown in Fig. 1. The sample was placed in an airtight container which was rotated about an axis making an angle of 54° 44′ with the steady magnetic field of about 4,740 gauss. The satellite lines were scarcely distinguishable from the noise background and the central spectrum consists of two sharp lines of approximately equal intensity. It is known from the X-ray diffraction examination by Clark, Powell and Wells[4] that in the solid state phosphorus pentachloride consists of equal numbers of tetrahedral $(PCl_4)^+$ and octahedral $(PCl_6)^-$ ions arranged on a tetragonal lattice. It is therefore reasonable to identify the two spectral lines with phosphorus nuclei in the two types of ion, the separation between the lines arising from their different chemical shifts. The spectrum has also been recorded in a field of about 3,550 gauss; the separation between the lines is found to be proportional to the field strength as the chemical shift explanation requires.

The chemical shifts of each line have been measured relative to the usual phosphorus standard, 85 per cent aqueous phosphoric acid, and are found to be +281 and −96 p.p.m. (The spectra were measured using a fixed field and a variable radiofrequency. The shift is therefore defined as $(\nu_r - \nu_c)/\nu_r$, where $\nu_c$ and $\nu_r$ are the frequencies for the compound and the reference respectively. This is equivalent to the usual definition $(H_c - H_r)/H_r$ when the frequency is held constant and the field is varied.) These shifts fall within the range +488 to −222 p.p.m. recorded for various liquid specimens[5]. Since there are equal numbers of the two types of phosphorus nuclei one cannot determine from the spectrum itself the assignment of the two lines to their respective ions. There is some indication that positive shifts arise when more than four atoms are connected to a phosphorus atom[6]. The shift for molecular $PCl_5$ in carbon disulphide solution is +80 p.p.m.[6] whereas for $PCl_3$ it is −215 p.p.m.[5]. The $(PF_6)^-$ ion, which like $(PCl_6)^-$ is an octahedral $sp^3d^2$ hybrid, has a shift of +148 p.p.m. in hexafluorophosphoric acid[7]. It seems likely, therefore, that the positively shifted line in solid phosphorus pentachloride arises from the $(PCl_6)^-$ ion, though this assignment cannot be certain. If the assignment is correct we have the following sequence of shifts in p.p.m. for four phosphorus chlorides: $PCl_3$ (−215), $PCl_4^+$ (−96), $PCl_5$ (+80), $PCl_6^-$ (+281).

We have found evidence that when the rotation-rate is a submultiple of the separation between the two lines, so that the satellites of each line are superposed on the central line and satellites of the other, there is an exchange of energy between the two systems of nuclei. This feature is being examined in more detail.

One of us (G. J. J.) wishes to thank the Chief Scientist, Department of Supply, Commonwealth of Australia, for enabling him to study at Bangor.

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## Line Breadths in the Ammonia Spectrum

The Van Vleck–Weisskopf formula for peak absorption and specified for the ammonia inversion spectrum in the microwave region can be written[1]:

$$\gamma_m = \frac{A}{\Delta\nu} f(J,K) \qquad (1)$$

where $A = \dfrac{6\pi^2 N f_1 \mu^2}{3ckT} \sqrt{\dfrac{B^2Ch^3}{\pi(kT)^3}}$

and $f(J,K) = g\dfrac{(2J+1)K^2}{J(J+1)}$

$$\nu_0^2 \exp\left\{-\frac{14\cdot3}{T}(J(J+1)-0\cdot366K^2)\right\}$$

There is evidence that $\Delta\nu$ varies with rotational state for the $J = K$ transitions as $\left(\frac{K^2}{J(J+1)}\right)^{1/n}$, where $n$ has the value[2] of either 2 or 3. If $\Delta\nu$ is normalized to the (3,3) line, as seems to be the present practice, then $f(J,K)$ in equation (1) should be multiplied by

$$\left(\frac{3J(J+1)}{4K^2}\right)^{1/n}, \quad n = 2 \text{ or } 3 \qquad (2)$$

The factor in equation 1 limiting an accurate prediction of intensity has been the value of $\Delta\nu$. Experimental intensity results have not previously warranted a more precise value of $\Delta\nu$. However, the development and construction of an improved microwave spectrometer at this University has allowed accurate measurements to be made on the intensities of absorption lines. A number of lines in the ammonia inversion spectrum have been measured ($J = K$, 1 to 6), and the results of these measurements are shown in Table 1. Column 3 lists the values predicted in Townes's "Microwave Spectroscopy"[4].

Table 1. Table of Peak Absorption Coefficients of Ammonia measured at $T = 27°$ C. and in the Pressure Region of 0·1–0·5 mm. Mercury

| $(J,K)$ | $\gamma_m$ measured ($\times 10^{-4}$ cm.$^{-1}$) | $\gamma_m$ calculated (ref. 6) ($\times 10^{-4}$ cm.$^{-1}$) |
|---|---|---|
| 1,1 | 1·81 ± 0·09 | 1·9 |
| 2,2 | 3·10 ± 0·11 | 3·2 |
| 3,3 | 7·87 ± 0·11 | 7·9 |
| 4,4 | 4·16 ± 0·03 | 4·3 |
| 5,5 | 3·87 ± 0·04 | 4·0 |
| 6,6 | 6·66 ± 0·08 | 6·9 |

The experimental values of $\gamma_m$ have been plotted against $Af(J,K)\left(\frac{3J(J+1)}{4K^2}\right)^{1/2}$ in Fig. 1. The value of the line-breadth parameter found from the straight line is:

$$\Delta\nu = 25{\cdot}7 \pm 0{\cdot}2 \text{ mc./s. per mm. mercury at } 27° \text{ C.}$$

The results of this experiment did not distinguish between the values of $n = 2$ and $n = 3$ in expression (2). The value of $n = 2$ was chosen because of its more generally accepted theoretical basis[5].

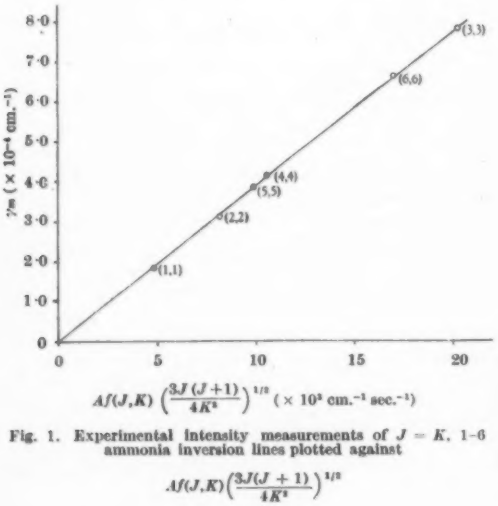


Fig. 1. Experimental intensity measurements of $J = K$, 1–6 ammonia inversion lines plotted against $Af(J,K)\left(\frac{3J(J+1)}{4K^2}\right)^{1/2}$

Yamano has measured $\Delta\nu$ and found it to be 27·5 ± 0·1 mc./s. per mm. mercury at 24·5° C. and to hold in the pressure region of 0·01–0·02 mm. mercury[6]. If $\Delta\nu$ is assumed to vary as $T^{-1}$ then under similar temperature conditions the value obtained here is some 2·3 per cent less than that of Yamano.

A more detailed report will be published in due course.

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## Sustained, Localized, Pulsed-Microwave Discharge in Air

Several recent publications[1–4] discuss possible methods whereby a localized gas discharge might be maintained by electromagnetic radiation. Recently a simple experiment to maintain an electrodeless discharge by focused microwave radiation was undertaken at this Laboratory. A small, localized discharge was obtained in low-pressure air. This discharge stands distinct and isolated from the generating apparatus and from any walls.

A pulsed, X-band radar transmitter is used as a microwave source. This unit emits pulses of approximately 0·5 μsec. duration, providing 40 W. average power and about 20 kW. peak power with an interpulse time of 290 μsec. These figures are nominal because stationary waves set up by the experiment cause deterioration of the magnetron. A pyramidal horn on the radar output is directed toward an 18-in. parabolic reflector 2 ft. away. An evacuated, roughly spherical glass chamber about 6 in. in diameter is placed at the focus of the paraboloid. A corona discharge from a Tesla coil is employed momentarily to provide the initial ionization within the chamber when the discharge does not occur immediately upon turning on the transmitter. A red or violet discharge is formed at the focus within the chamber. The size of the discharge is variable, the maximum dimension ranging from about 1 to 4 cm.

Several factors influence the appearance of the discharge. At pressures from about 3 to 20 mm. mercury its shape is irregular, exhibiting several striations. At higher and lower pressures, the discharge takes on the shape of one or two 'sausages' with their long axes in the direction of the electric vector of the microwaves from the transmitter. At about 0·3 mm. mercury, the lowest pressure at which it can be maintained, the discharge is red and diffuse. As the pressure is increased, the discharge gradually becomes definite in its configuration and violet in colour. At about 6 mm. mercury the colour is a bright violet and the edges are well defined. This remains true as the pressure is increased to 47 mm. mercury,

the highest pressure at which the discharge has been maintained.

Movement of the glass chamber modifies the shape of the discharge. This, as well as the striated appearance, is attributed to perturbations of the electromagnetic field by internal reflexions from the chamber walls. These reflexions can sometimes split the discharge into two or, rarely, three parts. However, the discharge does not move with the chamber. The position of the discharge is clearly determined by the transmitter-reflector geometry and can be obtained at any point within the chamber. If the discharge is brought into contact with the walls of the chamber, it will spread along a portion of the wall. If the focus is moved to the outside of the chamber, the discharge is extinguished.

There is no noticeable increase in the temperature of the chamber if the discharge is not brought in contact with the wall. When such contact occurs, the wall becomes warm and is uncomfortable to touch within 10 sec.

I wish to thank Messrs. Donald J. Ritchie and Carl P. Tresselt for their part in planning and carrying out these experiments.

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## CRYSTALLOGRAPHY

### Crystal Structure of $Ba_{0.5-x}TaO_{3-x}$

A STUDY of the barium–tantalum–oxygen system has produced the compounds $Ba_3TaO_{5.5}$ with an ordered perovskite structure[1], $Ba_5Ta_4O_{15}$ with a hexagonal layer structure[2], $Ba_{0.5}TaO_3$ with the tetragonal bronze structure[3], and $Ba_{0.44}TaO_{2.94}$, a hexagonal phase for which a trial structure has just been determined. The preparation of a powder and a single crystal of the reduced phase, $Ba_{0.44}(Ta^{IV}_{0.74}Ta^{V}_{0.26})O_{2.87}$, as well as analogous phases has previously been described[4]. It was later found that this reduced phase was produced only when the tantalum pentoxide used in the preparation was obtained from a particular source. The method of preparation is to mix appropriate quantities of tantalum pentoxide, tantalum metal, and barium oxide and heat in vacuum. Attempts to prepare larger amounts of the phase for density measurements after the original source of tantalum pentoxide was exhausted, were unsuccessful unless a barium chloride flux was added. The preparations obtained with the use of the flux, however, were not homogeneous, and good density measurements were therefore not obtained.

Single crystal studies indicate that the reduced phase has the same cell size ($a = 8{\cdot}96$ Å., $c = 7{\cdot}79$ Å.) and structure as the oxidized phase. Since crystals of the reduced phase were easier to prepare, they were used for the structure determination.

Intensities were obtained for $hk0$ and $h0l$ zones on a Buerger precession camera using molybdenum $K\alpha$ radiation. A sharpened $hk0$ Patterson projection was prepared. With the aid of a suggestion from Dr. A. D. Wadsley as to the possible structural relationship to $K_3V_8O_{14}$[5], it was seen almost at once that placing six tantalum ions in the positions $x$, 0, $\pm z$; 0, $x$, $\pm z$ and $\bar{x}$, $\bar{x}$, $\pm z$ with $x = 0{\cdot}23$ would account for the most important peaks of the vector map. These were the positions of 3/5 of the vanadium ions in $K_3V_8O_{14}$. The bariums were placed in the potassium positions, $x$, 0, $z$; 0, $x$, $z$; $\bar{x}$, $\bar{x}$, $z$, and $x$ was determined as about 0·63, by an $h00$ Fourier line projection. Of the possible space-groups only $P62m$ would allow these positions.

From the $00l$ data, it was determined that a reasonable fit could be obtained if three tantalums were placed at $z = 0{\cdot}25$, three at $z = 0{\cdot}75$, and three bariums at $z = 0{\cdot}50$. An $h0l$ Patterson projection and a subsequent $00l$ Fourier line projection showed that $z$ for the tantalums should be about 0·24 and 0·76 and the bariums should be at about $z = 0{\cdot}50$.

As for the oxygen packing the neatest arrangement would appear to be oxygens directly above and below each tantalum (a scheme that accounts so well for the axial length) and oxygens at the same $z$ values as tantalum to make groups of three corner-sharing octahedra. The approximate co-ordinates for the atoms so obtained are given in Table 1.

Table 1

| Atoms | $x$ | $y$ | $z$ |
|---|---|---|---|
| 3 Ba in ($g$) | 0·63 | 0 | 0·50 |
| 6 Ta in ($i$) | 0·23 | 0 | 0·24 |
| $3O_1$ in ($g$) | 0·23 | 0 | 0·50 |
| $3O_2$ in ($f$) | 0·23 | 0 | 0 |
| $3O_3$ in ($i$) | 0·84 | 0 | 0·24 |
| $12O_4$ in ($l$) | 0·47 | 0·18 | 0·24 |

Using the above parameters for the atoms a fair fit was found for observed and calculated $hk0$ and $00l$ structure factors ($R = 0{\cdot}24$).

The following points are disturbing about the trial structure: (1) There are marked deviations from Pauling's electrostatic valence rule in that the sum of strengths of electrostatic bonds to oxygens from adjacent cations is as low as 1·23 for some oxygens and as high as 2·27 for others. (2) The trial structure leads to an empirical formula of $Ba_{0.5}TaO_3$ with no obvious explanation of the observed fixed ratio of Ba : Ta of about 0·44. (3) There are only 18 oxygens occupying 24 crystallographically available positions (still fewer in the reduced phase), thus leaving considerable unfilled volume, again for no obvious reason. (4) The X-ray density based on the trial structure is lower than the observed range of values.

The obvious thing to try would be the inclusion of a greater number of cations, and therefore oxygens, in the structure. Judicious placement of the additional cations could favourably change the situation with respect to all the points raised above. However, so far, all attempts to add atoms to the structure have led to a greater deviation of observed from the calculated structure factors.

It is hoped that we shall be able to collect more complete data on this compound. Our intention is then to substitute a machine Fourier approach, with the described trial structure as a starting point, for the human semi-logical semi-intuitive approach we have so far been using. (It may be pointed out that this latter approach is somewhat handicapped because the structure is non-centrosymmetric.) Should these efforts prove fruitful, the results will be reported at another time.

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## GEOLOGY

### Spectral Reflectivity of Ore Minerals

It would appear that there may have been some ambiguity in the use of the terms 'standard reference surfaces' and 'standard values' in our recent article on the above subject[1]. The standard reference surfaces specifically refer to a polished basal section of quartz and to liquid mercury under a coverslip, which were measured for us by the National Physical Laboratory. The intention was that these two surfaces would be readily reproducible by other workers. The confusion has arisen in that two other surfaces of intermediate reflectivity were also measured for us by the National Physical Laboratory to assist in the calibration of our equipment. It is entirely incidental that these two 'other surfaces' were hæmatite and pyrite; their identity is immaterial and the values of reflectivity quoted for them are not standard values, *sensu stricto*, since minerals will, in many cases, show a range of reflectivit due to variable compositjon and optical anisotropy.

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## GEOCHEMISTRY

### Pigments of a Fossil Echinoderm

Several years ago, I described[1] the discovery of crystallized organic pigments ('fringelite') in a fossil crinoid (*Millericrinus*) of upper Jurassic age. Additional specimens have now been collected at the two original locations (Fringeli and Liesberg, both in north-western Switzerland). The pigments are isolated by solvent extraction and separated by repetitive chromatography and fractional crystallization. Six pigments (fringelite *A*–*F*) have been isolated: additional pigments remaining in the fossil after exhaustive extraction with pyridine can be dissolved in concentrated sulphuric acid in which they exhibit an absorption spectrum similar to that of the more soluble fringelites. All these pigments are similar in respect to their absorption spectra, the colour of their solutions (red in organic solvents, green in sulphuric acid), the formation of green, insoluble sodium salts and the ease with which acetyl- and benzoyl-derivatives are formed. In all these properties the fringelites strongly resemble extended quinones of the type of aphin[2] or hypericin[3].

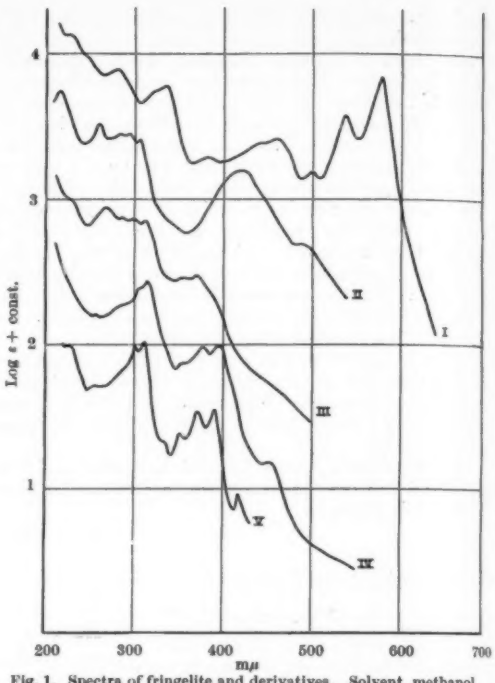


Fig. 1. Spectra of fringelite and derivatives. Solvent, methanol. I, Fringelite *E*; II, acetyl derivative of fringelite *E*; III and IV, hydroacetyl derivatives; V, fossil alkyl-benzperylene

They even give the characteristic aphin-reaction, a blue(-violet) colour, on treatment with acetic anhydride containing a small amount of sulphuric acid.

The visible and ultra-violet absorption spectrum of fringelite *E* in methanol (Fig. 1, curve I) shows a general resemblance to that of erythroaphin *fb* (ref. 4); however, differences in band positions and relative extinctions of the band systems at 450 and 550 mμ indicate the presence of a similar but not identical chromophoric system. The acetyl-derivative of curve II is obtained by exhaustive acetylation with pyridine-acetic anhydride. Hydroacetyl derivatives (curves III and IV) are formed by reduction with zinc dust in the same medium. Curve IV, except for a displacement to longer wave-lengths (amounting to 13·5 mμ for the main band at 298·5 mμ and 8 mμ at 383 mμ, both in methanol), is nearly identical with that of the 6-ring aromatic hydrocarbon 1.12-benzperylene; curve III shows the typical bands of highly substituted phenanthrenes. The same phenanthrene band system is also evident in curve II (the acetyl pigment) in addition to absorption at longer wave-lengths caused by the carbonyl groups of the quinone.

From these spectral data we conclude that the fringelites are polyhydroxyquinones of 1.12-benzperylene. The aromatic hydrocarbon is substituted by the quinone oxygens in such a way that three aromatic rings with phenanthrene configuration remain undisturbed. By hydrogenation this quinone is reduced to the hydroquinone with the benzperylene spectrum IV, which, by more vigorous treatment, is transformed into the phenanthrene-derivative III.

The ultimate reduction products obtained in the laboratory and in Nature provide further proof for

this structure. Zinc-dust fusion[5] leads to 1.12-benzperylene-type hydrocarbons of varying degrees of substitution, in addition to small amounts of a pyrene derivative. An alkyl-benzperylene also occurs naturally in the fossil sea lily[1].

The various fringelites seem to differ mainly in the number and position of their hydroxyl groups. The spectral data and the formation of a pyrene-derivative in the zinc-dust fusion suggest that the quinone-oxygens are located in 4 and 9 positions. The presence of alkyl substituents, the position of which is not yet clear, is indicated by a considerable spectral band shift from the synthetic benzperylene to the fossil hydrocarbon and the products of the zinc dust fusion. However, the 6 and 7 positions do not seem to be bridged by an alicyclic ring or substituted by an alkyl-chain since coronene is not formed in the zinc-dust fusion.

It has been suggested[6] that the pigments of recent crinoids are closely related to the hydroxynaphthoquinones of other echinoderms (echinochromes, spinochromes). In my previous paper I had suggested that the fringelites and the fossil benzperylene are the products of successive redox and condensation reactions between two echinochrome molecules, a hypothesis that has been further corroborated by the present findings. Fringelite *F* and the even more polar materials soluble only in concentrated sulphuric acid would be the primary condensation products; they are also the major pigments (several gm./kgm. of the fossil). The small amounts of the less polar pigments (mgm./kgm. for fringelites *D* and *E* and μgm./kgm. for pigments *A*, *B* and *C*) and the hydrocarbon have been formed from the major pigments by reduction and elimination of substituents.

The highest pigment concentration occurs in the massive (2–3 in. diameter) roots and lower parts of the stem; small stems (½ in. diameter) and crowns rarely contain more than traces of pigments. Other fossils of the same locations, including small sea urchins and their spines, are completely devoid of pigments. Apparently, conditions for the preservation of the pigments were sufficiently good only below the sediment-water interface where the roots and heavy stems accumulated during or immediately after the lifetime of the crinoids.

Discovery of the fringelites is geochemically significant, permitting for the first time the reconstruction of a complex reaction sequence, involving reduction, condensation, oxidation and further reduction and elimination of substituents under the final formation of a polynuclear aromatic hydrocarbon. A knowledge of such transformation reactions permits conclusions about the chemical environment and the organic reactivity in the sub-surface.

A more detailed report of this work is being prepared for publication in *Geochimica et Cosmochimica Acta*. This investigation has been supported by a research contract with the United States Office of Naval Research (Contract *NONR*-2196 (00)).

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## Exposure Ages for Iron Meteorites

Schaeffer and Fisher[1] have given values for the exposure ages (that is, the time during which the meteorites were exposed to cosmic rays after having been broken out of a bigger body) of 18 iron meteorites. These ages vary between $20 \times 10^6$ to $1{,}900 \times 10^6$ years. I think these authors have made some mistakes in interpreting the results of their experimental work.

Exact determinations of the exposure ages of meteorites are only possible by combining the values of a stable and a radioactive cosmic-ray spallation product. For measurements of radioactive spallation products big samples are needed, and therefore only few such determinations were made. If one knows the size of the meteorite before passing the Earth's atmosphere and the location of the sample analysed inside the meteorite, it is possible to calculate the exposure age from the content of any stable spallation product alone. Unfortunately, we do not know the location of the samples or, better, their distance from the original surface of the meteorites.

Schaeffer and Fisher tried to calculate the 'depth' of the samples from the ratios of the content of different stable spallation products and based this calculation on two assumptions:

(1) The energy spectrum of the particles which produce nuclear spallation varies with the distance from the surface and with the size of the meteorite. Because of the secondary particles which have relatively low energies, the mean energy of the particles producing spallations decreases with the depth from the surface.

(2) The ratio of helium-3 to argon-38 is a measure for the mean energy of the particles.

Schaeffer and Fisher used this ratio to calculate the depth of the samples analysed and then determined from the total amounts of helium-3 the exposure ages of the meteorites.

There are errors in both of these assumptions.

(1) The energy spectrum of the primaries extends from at least 500 MeV. to several BeV. Especially from data on meteorites an extension down to about 200–300 MeV. seems very probable[2,3]. These low-energy primaries lie in the same energy-range as the secondaries. For particles of this energy-range of several 100 MeV., the diminution by loss of energy through ionization and excitation is not negligible apart from the diminution by nuclear absorption. By this loss of energy the mean energy of the primary particles increases with the distance passed in the meteorites. This increase of the mean energy of the primaries is balanced in big meteorites by the low-energy secondaries; and even the ratio of the flux of the secondaries to the flux of the high-energy primaries (with energies $> 1$ BeV.) reaches a nearly constant value already for a depth of about 30 cm. caused by the diminution of the secondaries by loss of energy through ionization and excitation[3].

(2) The ratio helium-3/argon-38 seems not at all a good measure for the energy of the particles which produce the spallation processes. This ratio should be nearly independent of the particle energy[4–6].

As neither assumption can withstand intensive examination, the exposure age based on them cannot be correct.

Some exact determinations of the exposure ages of meteorites are known, for which Schaeffer and Fisher

also have given values. Fireman[7], measuring argon-39 and helium-3, found the same age for Treysa and Sikhote–Alin meteorites; nearly the same results were found by me[8,9]. Schaeffer and Fisher, however, gave the age of Treysa as being more than ten times higher than that of Sikhote–Alin. I have also tried to find at least approximate values for the exposure ages of iron meteorites from the results of stable spallation products only; these results will be published in due course.

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In our communication it was pointed out that it is possible to estimate a cosmic-ray exposure age for a meteorite from a measurement of the stable rare gas contents alone. The difficulty with such estimates in the past has been that it was not possible to estimate the cosmic-ray production-rate of a stable nuclide in the particular sample of the meteoroid measured, as the production-rate depends on the unknown depth of the measured sample in a meteoroid of unknown size. The proposed estimate of production-rate was made from the observation that for meteorites with low argon-39 and chlorine-36 activity (that is, low cosmic-ray nuclide production-rates) the ratio helium-3/argon-38 is lower than in meteorites with high argon-39 and chlorine-36 activities. It was also pointed out that the same is true for the ratios helium-3/helium-4 and neon-21/argon-38. The discussion of the dependence on energy of these ratios was included to give a possible explanation for the observed dependence. The only assumptions made were that the dependence is not a coincidence or an experimental error. This argument has been discussed by Wänke in the preceding communication. Contrary to Wänke's statement, the estimation of the exposure ages is not based on assumptions concerning the energy spectrum of the cosmic-ray particles producing the rare gases or on whether the ratios are a measure of the mean energy. The estimation is based only on experimental observations which indicate a relationship between the ratios helium-3/argon-38, helium-3/helium-4, neon-4/argon-38 and the production-rate of the radioactive nuclides chlorine-36 and argon-39 by cosmic rays.

The relationship found is to be expected from the results of the measured proton-production cross-sections cited by Wänke[1,2]. It was found that the proton-production ratio $\sigma_{He} + \sigma_T/\sigma_{Ar^{38}}$ (which is to be compared to helium-3/argon-38 in meteorites) changes from about 8 with 400 MeV. protons to 23 with 3 BeV. protons; while the proton-production ratio $\sigma_{He^3} + \sigma_T/\sigma_{He^4}$ changes from 0·19 at 400 MeV. to 0·26 at 3 BeV. The results on the neon production are at present too fragmentary for a comparison; however, from the systematics of spallation processes (Friedlander, G., private discussions and ref. 3) it is to be expected that the ratio neon-21/argon-38 will show a similar change. These cross-section measurements indicate that the proton-production ratios helium-3/argon-38, helium-3/helium-4 and neon-21/argon-38 change with proton energy and lead one to suspect that this is the reason for the variation of the ratios in meteorites.

On the other hand, more recent, but preliminary, results[4] indicate that the ratio helium-3/argon-38 does not vary with energy. In addition, recent measurements of Signer and Nier[5] indicate that in a given meteorite the ratio helium-3/argon-38 is constant to at least 5 per cent while the helium-3/helium-4 and neon-21/argon-38 ratios vary by about 15 per cent. Both these observations are in agreement with Wänke's statement that the ratio helium-3/argon-38 is not a good measure of the mean energy of the particles.

If this view is substantiated by further experiments, then the observed relation between cosmic-ray production-rates and the helium-3/argon-38 ratio must have some other explanation. For example, as pointed out by Wänke, the ratios of primary to secondary particles may vary depending on the meteorite size or location of the sample inside the meteoroid. In any event, the use of the helium-3/argon-38, helium-3/helium-4 or neon-21/argon-38 ratio to estimate a cosmic-ray production-rate is based on an empirical relationship and can be disproved only by further experiments.

This work was carried out under the auspices of the U.S. Atomic Energy Commission.

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## CHEMISTRY

### Crystal Structures of 1-Chloro-2,4-Dinitrobenzene and 1-Bromo-2,4-Dinitrobenzene

The rates of reaction for nucleophilic aromatic substitution are affected if the replaced group has one, or two, groups ortho- to it. In particular, the effects of nitro groups in these positions (and in meta- and para-positions) have been studied in many reactions. Generally, these groups contribute two competing effects which control the reaction-rate. First, a maximum activation through electron transfer is attained if the nitro group is planar with the benzene ring. However, spatial considerations often forbid this coplanarity in the case of ortho-substitution, and there exists a competing de-activation due to the twist of the nitro group from the plane of the benzene ring. In the extreme case of two ortho-substituents, the activating effect of the nitro groups

is greatly diminished by this steric effect and may result in a net de-activation.

The reaction-rates of many nucleophilic reagents with 1-halo-2,4-dinitrobenzenes have been measured in several laboratories[1-4] and a comprehensive review of the subject of nucleophilic substitution reactions and their mechanism has been published by Bunnett[5]. Kruger and Bednova[1] showed that, although chlorine normally accelerates reaction, the acceleration was weaker when it was ortho- to an activating nitro group, when reactions of methoxide with 1-chloro-2,4-dinitrobenzene were studied. The de-activation was attributed to rotation of the nitro group, thus interfering with the partial conjugation of the C—N bond. Parker[6], again investigating reactions of methoxide and 1-halo-2,4-dinitrobenzenes, observed these steric effects and found the order of de-activation to be I > Br > Cl > F, and suggested that this was due to the relative sizes of the halogen atoms causing varying angles of rotation of the ortho-nitro groups. As no direct measurements of the molecular dimensions of these molecules had been made, it was suggested by Dr. J. Miller, of the Department of Chemistry, University of Western Australia, that single-crystal X-ray diffraction structure analyses of the 1-halo-2,4-dinitrobenzenes be undertaken to measure accurately these angles of twist of the 2-nitro groups. Samples of the chloro-, bromo-, iodo- and fluoro-compounds were kindly provided by Dr. J. Miller for the investigation.

Preliminary studies of the compounds showed two of them, 1-chloro-2,4-dinitrobenzene and 1-bromo-2,4-dinitrobenzene, to be isomorphous, conforming to the orthorhombic space-group *Pccn* and having eight molecules in the unit cell. 1-iodo-2,4-dinitrobenzene crystallizes in a lower symmetry and 1-fluoro-2,4-dinitrobenzene is a liquid at room temperature.

The chloro- and bromo-compounds were chosen for initial detailed study. Their cell dimensions are :

| Compound | $a_0$ | $b_0$ | $c_0$ |
|---|---|---|---|
| 1-Chloro-2,4-dinitrobenzene | 8·937 Å. | 11·035 Å. | 15·675 Å. |
| 1-Bromo-2,4-dinitrobenzene | 8·898 Å. | 11·244 Å. | 15·753 Å. |

Intensity data up to sin $\theta/\lambda = 0{\cdot}515$ for the ($0kl$) and ($h0l$) zones of both compounds were measured on a single-crystal Geiger counter spectrometer. These were extended to the full range of the sphere of reflexion for copper radiation by standard photographic techniques.

The heavy-atom co-ordinates were found from Patterson and difference Patterson syntheses projected on the (100) and (010) planes. The remaining atomic positions were located in Fourier syntheses on these planes, the signs of the Fourier coefficients being determined, initially, by the contribution of the heavy atom alone and then, later, by the combined contributions of the heavy atom and seven postulated light atoms.

The (100) and (010) projections of both compounds have been refined by successive difference syntheses and the 'reliability indices' for the calculated and observed structure factors are $R$ ($0kl$) = 0·137 and $R$ ($h0l$) = 0·118 for 1-chloro-2,4-dinitrobenzene and $R$ ($0kl$) = 0·097 and $R$($h0l$) = 0·087 for 1-bromo-2,4-dinitrobenzene.

As expected, the planes of the 2-nitro groups are rotated from the planes of the benzene rings, the measured angles being 39° for the chloro-compound and 40° for the bromo-compound. The proximity of the 2-nitro groups and the heavy atoms in these compounds has also caused distortions of the heavy atoms from the positions collinear with the 1- and 4-carbon atoms of the benzene rings. Thus the $C_1$-Hal bond is at about 5° to the line joining $C_1$ and $C_4$.

In addition, the planes of the 4-nitro groups are rotated from the planes of the benzene rings. These twists (about 15°) are presumably due to field effects associated with the neighbouring molecules.

The average bond-lengths at the present stage of refinement are 1·20 Å. for the N—O bonds and 1·45 Å. for the C—N bonds.

Assumptions attributing chemical de-activation of these compounds to the rotation of the ortho-nitro groups out of the benzene ring planes have been found to be justified stereochemically. However, the conclusion of Parker[6] regarding the relation of the relative twists of these groups and their de-activating powers has not been verified.

Although all the points of chemical interest in the structures have now been elucidated, evidence for thermal anisotropic motions of the heavy atoms and the atoms of the nitro groups has appeared in the difference maps. An analysis of these vibrations is in progress and a full report will shortly be published elsewhere.

During the course of these X-ray investigations a brief preliminary report of an investigation of the structure of 1-chloro-2,4-dinitrobenzene was published[7], but the results of only one projection were given, and there was consequently no discussion of the chemical significance of the results.

Financial assistance provided by the Australian Atomic Energy Commission is gratefully acknowledged.

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## Magnetic Resonance of Protons in Glasses

We have been interested in the effect of sodium fluoride and calcium fluoride on molten silicates and phosphates, and the principal reactions are being investigated using kinetic and infra-red techniques. We have also been interested in the elimination of water from the melts by the fluorides and have used a proton magnetic resonance technique for studying the elimination. The infra-red technique has recently been used to investigate water elimination from silicate-glasses[1], but it would be difficult to obtain results using the same technique for glasses containing phosphate since these pick up water to a great extent and very quickly.

Sodium metaphosphate and potassium metaphosphate can be prepared by heating the sodium and

potassium dihydrogen phosphates respectively. The metaphosphates are produced from their respective acid salts by dehydration processes; hence to prepare these compounds containing water it is only necessary to heat the acid salts for a short time. The sodium metaphosphate glass and potassium Kurrol salt were prepared by heating the respective A.R. quality salts for 6 min. at 900° C. Similarly, borate-glass containing water was prepared by heating A.R. ortho-boric acid for 6 min. at 900° C.

Mixtures of sodium disilicate and sodium metaphosphate plus sodium disilicate and sodium pyrophosphate were saturated with water by heating the melts in a stream of steam at 1,000° C. for 8 hr. Carefully dried, analytical reagent quality sodium fluoride was added to each of these samples to give 10 weight per cent mixtures and the mixtures heated in attempts to eliminate the water.

Samples were quenched on a clean stainless steel plate and immediately crushed and weighed out in dry boxes maintained at 30–35 per cent relative humidity. 1-gm. samples were sealed in 'Pyrex' tubes which had been carefully dried at 400° C. for two to three days. During the sealing process, the 'Pyrex' tubes were connected to a drying tower containing phosphorus pentoxide, so the sample was not exposed to the air.

Proton resonances were observed using a Pound–Watkins marginal oscillator of conventional design operating at a fixed frequency of 21·750 Mc./s. The magnetic field was varied by connecting a motorized d.c. supply across field-bias coils wound around the poles of a permanent magnet. Tuning of the radio-frequency amplifier stage was employed to facilitate production of low oscillation-levels. The field was modulated at 280 c./s. and the output of the marginal oscillator passed through a phase-sensitive detector to give a derivative signal to a chart recorder.

The specimens were found to be easily saturated, and the resonance signals were therefore rather weak. Line-widths were about 4 œrsteds, and a modulation amplitude of 1·5 œrsteds was found to give optimum signal-to-noise ratio. The oscillation amplitude was maintained at a constant level corresponding to about 100 mV. across the specimen coil. A 5-sec. time-constant filter was used in the output stage of the phase-sensitive detector.

The signal strength was taken as the distance between maximum displacements of the derivative curve. It was estimated that any water content exceeding ¼ per cent would give a resonance signal detectable with this apparatus.

In the sodium metaphosphate series, samples of the glass were heated for 5, 10 and 20 min. with sodium fluoride. The proton signals are shown in Fig. 1 and it can be seen that the water, which is bonded in the lattice, is eliminated.

Similarly, water is eliminated by sodium fluoride from potassium Kurrol's salt, boron trioxide and the disilicate–metaphosphate mixture containing 15 per cent phosphorus pentoxide.

Further, an estimate of the accuracy of the determination of the number of protons by the resonance method was made by preparing two samples of boron trioxide in which the water content can be determined by titration[2]. The ratio of water contents in the samples by direct titration and the ratio of signal-to-noise ratio for the two samples are 3·4/2·8 and 8·3/6·5 respectively. We have also located

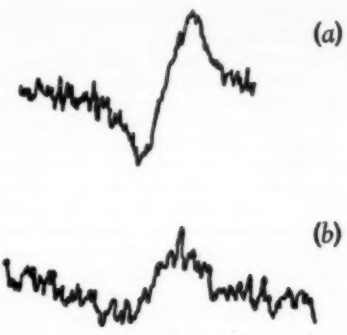


Fig. 1. (*a*) Proton resonance at 21·750 Mc./s. due to water in sodium metaphosphate glass.
(*b*) Proton resonance at 21·750 Mc./s. in the same sodium metaphosphate glass after being heated at 900° C. for 5 min. with dry A.R. quality sodium fluoride

proton resonance peaks in the other phosphate-silicate mixtures prepared.

Attempts to use the fluorine-19 chemical shift to determine the amount of P–F and Si–F bonding in the various samples were unsuccessful.

These results will be reported in more detail later.

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## Atomic Polarizations of Chloro-, Bromo- and Iodo-benzene

In 1940, Bottcher[1] suggested that the distortion polarization of a compound such as mono-chlorobenzene might be obtained by assuming it to be the mean of the total polarization for the parent compound, benzene, and for *p*-dichlorobenzene.

Dielectric constant and density measurements on benzene, chlorobenzene, *p*-dichlorobenzene, bromobenzene, *p*-dibromobenzene, iodobenzene and *p*-diiodobenzene, using carbon tetrachloride as solvent at 25°, have been made and the distortion polarizations of chloro-, bromo- and iodo-benzene calculated.

The atomic polarizations obtained by subtracting the electronic polarizations ($R_D$) from the distortion polarizations ($P_D$) determined in this manner are given in Table 1 under the heading $P_A$ (exp.).

Table 1

| Compound | $P_A$ (exp.) (c.c.) | $P_A$ (calc.) | 0·05 $R_D$ |
|---|---|---|---|
| Chlorobenzene | 3·7 ± 0·4 | 2·8 | 1·6 |
| Bromobenzene | 2·5 ± 0·5 | 2·1 | 1·7 |
| Iodobenzene | 2·4 ± 0·7 | 1·8 | 2·0 |

The respective in-plane and out-of-plane bending frequencies (ν) for the mono-halogenobenzenes, as assigned by Pyler[2], have been substituted into an equation for a much simplified model of a halobenzene molecule. For this model the halogen

atom ($X$) is regarded as the 'bob' of a simple pendulum of length $r$, equal to the (aromatic) C—$X$ distance; the bending force constants for the two bending modes is calculated from $k_B = 4\pi^2\nu^2 m_x$. When such values of $k_B$ are substituted into the equation $P_A = (4\pi N\mu^2/3k_B)$ and these $P_A$ values are added to the atomic polarization figure for benzene (1·6 c.c.), the $P_A$ (calc.) figures listed in Table 1 are obtained.

Also listed in Table 1 are the estimates often used for the atomic polarizations, namely, that they are 5 per cent of the electronic polarizations.

Bottcher's method, when applied to the three mono-halogenobenzenes, gives values for the atomic polarizations of these molecules, which are in qualitative agreement with rough application of theory. Further, it indicates a decrease in atomic polarization with increasing mass of substituent in the series chloro-, bromo-, iodo-benzene, thus lending support to the idea[4] that atomic polarization cannot be assumed to be a fixed fraction of the electronic polarization of a molecule.

Details of this work will be published elsewhere.

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## Ionic Conductances in Gels of Wheat Starch

Polymeric gel systems may be formed either by cooling a polymer solution, or by swelling a suspension of solid polymer particles in a suitable solvent. These two types of gelation process differ in one fundamental respect. Gel formation from solution is usually a thermoreversible process, and on warming, the system reverts back to a solution. On the other hand, gelation by swelling is thermally irreversible, and scarcely any shrinkage occurs on cooling.

Starch gelation in water is a typically irreversible process. Above 55°, granules of wheat starch swell irreversibly. On cooling, molecules from adjacent granules link up by hydrogen bonding and molecular entanglement to form a continuous network of swollen starch granules.

There is evidence in the literature[1,2] that gel formation from solution occurs with little or no change in the conductance of electrolyte present. This means that the water has a micro-viscosity similar to that of normal free water, although of course the bulk viscosity of the gel is considerably greater. However, it has previously been shown from the nuclear magnetic resonance spectra[3] that starch gelation has a very marked effect on the water structure. These changes should be reflected in the conductance, and it was therefore decided to study the conductance changes of sodium chloride in a number of starch–water mixtures during gelation. Conductivity measurements were made using a pair of platinum disk electrodes. The mixtures were heated slowly from 25° to 85° and afterwards cooled back to 25° again. During the early period of heating

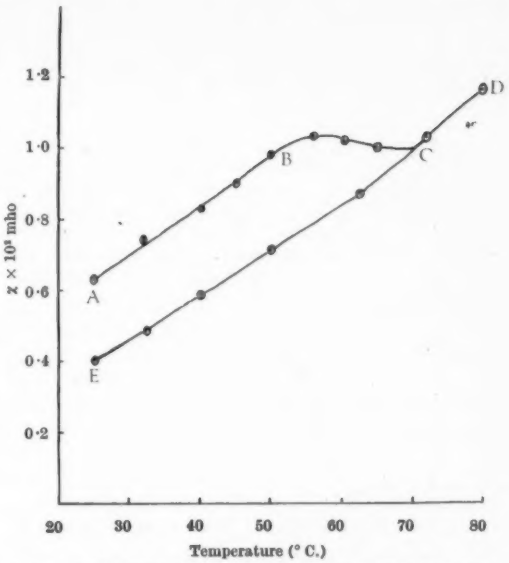


Fig. 1. Conductance of 0·412 per cent sodium chloride in 37 per cent starch

the system consisted of two phases, and the suspension was agitated before readings were taken. Above 55° gelation took place and the electrodes became firmly embedded.

Provided there was sufficient starch (12 per cent) to form a coherent gel, the conductances were always lower in the gel than in the suspension as expected. A typical example is shown (Fig. 1) in which the changes can be conveniently divided into three portions.

(1) The suspension $AB$ before gelation has started. During this stage the changes in conductance are thermally reversible.

(2) The process of gelation $BC$ during which the conductance falls. Gelation is an irreversible process and the line $CB$ cannot be retraced if the system is cooled. On cooling from a point on $BC$, the conductance values fall on a line intermediate between $AB$ and $EC$.

(3) The fully gelatinized system $ECD$. Gelation is complete at $C$ and the conductivity starts to rise again with increasing temperature. The conductance is now thermally reversible, and on heating or cooling, the conductance values will always lie on the same curve $ECD$.

These changes in conductance can be correlated with the swelling behaviour of wheat starch. At 25° water is absorbed into the amorphous regions, and the granules swell about 30 per cent by volume[4]. Little further swelling occurs until about 55° when the granules suddenly begin to swell rapidly with increasing temperature[5]. This is the point $B$ where the gel is first formed, at high starch concentration. The process of swelling and particle adhesion continues for about another 15°, the maximum swelling (at $C$) being governed by the amount of water available.

Having established the general pattern of behaviour, some more precise conductance ($\chi$) measurements were made on suspensions and gels containing 37 per cent starch and varying amounts of sodium chloride, at 25° and 50°. Corrections for ionic

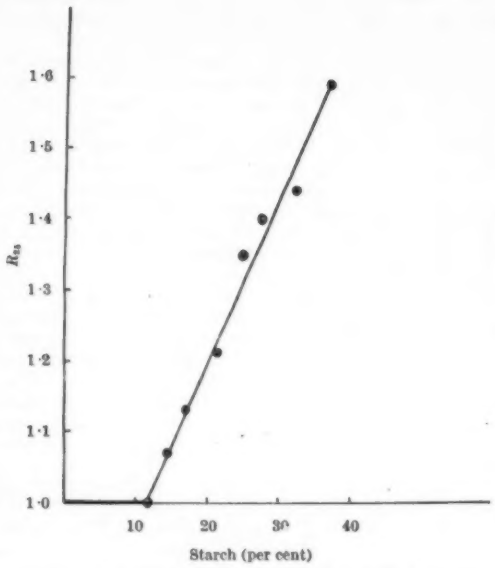


Fig. 2. Variation of $R_{25}$ with starch concentration

impurity in the starch were made, by subtracting the values obtained during a blank experiment done in the absence of any added sodium chloride. The corrected results are given in Table 1 and Fig. 2.

It was found that $\frac{1}{\chi}\frac{\Delta\chi}{\Delta T}$ (and consequently the energy of activation for ionic mobility) over this temperature-range was 1·7 times greater in the gel than in suspension. This is in qualitative agreement with the increase in the micro-viscosity of the water after gelation, which has previously been established from the water proton line in the nuclear magnetic resonance spectra. The band-width of this line was found to increase on gelation, and there was no 'free' water line superimposed on the broader line. Therefore, all the water in the gel is in a more highly bound state, leaving no fibrils of free water, contrary to what has been postulated for some other gel systems.

The variation of the conductance behaviour with starch concentration follows a pattern similar to the variation of nuclear magnetic resonance water band-width. The ratio of conductance of sodium chloride in suspension and gel at 25° ($R_{25}$) increases almost linearly from 1·0 at 12 per cent to 1·6 at 37 per cent starch, showing that the water becomes increasingly bound as the starch concentration is increased above 12 per cent. Similarly the water proton line in the nuclear magnetic resonance spectra resembles that of pure water in swollen starch mixtures up to about 12 per cent concentration, but at higher concentrations the band-width increases. The similarity between these two sets of results suggests that the change in the water structure on gelation is the main factor contributing to the fall in conductance.

There may also be other factors. For example, it is possible that the ions do not penetrate into the granules, in which case the tortuous migration of ionic particles around the swollen granules would tend to reduce the conductance. However, it is known that some large molecules, for example the dye congo red, are easily absorbed by swollen granules even in the cold, and it therefore seems likely that sodium chloride penetrates into the granules. This is supported by the fact that swelling causes no detectable drop in conductance ($R = 1$) at starch concentrations just below the minimum starch concentration (12 per cent) for gel formation, where the swollen granules occupy about 50 per cent of the total volume.

It seems likely that these unusual conductance results are due primarily to the change in water structure. If this is so, the ratio $R_{25}$ should be a rough measure of the micro-viscosity of the water in the gel, since the conductivity is approximately inversely proportional to the viscosity of the medium.

The increase in micro-viscosity on gelation has, on the basis of the nuclear magnetic resonance results, previously been attributed partly to the formation of a four co-ordinated water lattice around each starch hydroxyl group, and partly to the 'fixing' of these regions of solvated water, by the formation of a continuous polymer network on gelation. Both these factors become more marked at higher starch concentrations; this is reflected in the increase in $R_{25}$. It is worth pointing out that gelatin, which is itself ionic, shows no fall in conductance on gelation[1]. This is probably because gelatin has a smaller effect on the water structure due to its lower hydrogen bonding power and also because the polymer concentrations are lower in these gels. The anomalous behaviour of starch is due to its high degree of hydrogen bonding power, which has a marked effect on the water structure and also enables the starch to form a strong polymer network.

Table 1. Conductance of Sodium Chloride in 37 per cent Starch

| Sodium chloride (per cent) | 0·206 per cent | 0·412 per cent | 0·824 per cent | 1·647 per cent |
|---|---|---|---|---|
| $R_{25}$ | 1·64 | 1·62 | 1·51 | 1·50 |
| $C_g$ | 0·026 | 0·030 | 0·028 | 0·027 |
| $C_s$ | 0·016 | 0·015 | 0·016 | 0·016 |
| $C_g$ / $C_s$ | 1·6 | 2·0 | 1·75 | 1·7 |

$R_{25}$ = Sodium chloride conductance in suspension at 25° / Sodium chloride conductance in gel at 25°

$C_g = \frac{1}{\chi}\frac{\Delta\chi}{\Delta T}$ for gel between 25° and 50°.

$C_s = \frac{1}{\chi}\frac{\Delta\chi}{\Delta T}$ for suspension between 25° and 50°.

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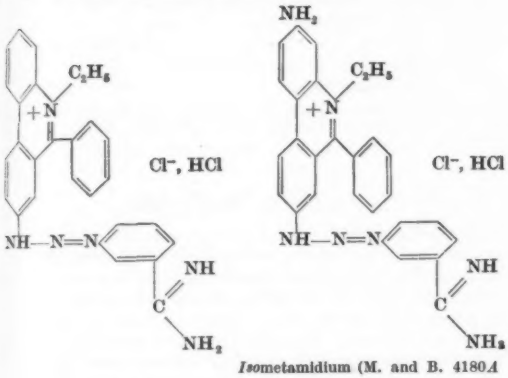
## BIOCHEMISTRY

### Structure of *Iso*metamidium (M. and B. 4180*A*), 7-*m*-Amidinophenyldiazoamino-2-amino-10-ethyl-9-phenylphenanthridinium Chloride Hydrochloride, the Red Isomer present in Metamidium

The trypanocidal drug, metamidium, first described by Wragg, Washbourn, Brown and Hill[1], was obtained from the coupling reaction between *m*-amidinobenzenediazonium chloride and homidium chloride. It was isolated as a mixture of purple and red compounds (55 and 45 per cent, respectively) which were

separated by fractional crystallization and shown to be isomeric. The red (M. and B. 4180*A*) was more active than the purple isomer, both therapeutically and prophylactically, against a laboratory strain of *Trypanosoma congolense* in mice. Wragg *et al.*[1], on the evidence available at the time, provisionally assigned diazoamino structures to these two isomers, and stated that work to verify these was being done. Several unsuccessful attempts were at first made to determine the structure of the red compound, and this has now been achieved by deamination which gave the desamino compound (I), which was identical in analysis, properties, and infra-red spectra with authentic specimens of (I) prepared by: (*a*) the coupling reaction of diazotized 7-amino-10-ethyl-9-phenylphenanthridinium chloride with *m*-aminobenzamidine, and (*b*) the coupling reaction of 7-amino-10-ethyl-9-phenylphenanthridinium chloride with *m*-amidinobenzenediazonium chloride.




(I) *Iso*metamidium (M. and B. 4180*A* (II)

The evolution of nitrogen which occurred when the red and purple compounds were heated with 6 *N* sulphuric acid was given as evidence for the presence of a diazoamino group in both compounds (Wragg *et al.*[1]), although it was pointed out by these workers that for unexplained reasons the purple isomer gave considerably less than the theoretical volume of nitrogen. Further work has now shown that these reaction conditions were too drastic for a diagnostic test for the presence of a diazoamino group as distinct from an aminoazo system, and milder conditions will clearly differentiate the two systems. Thus, if the red compound (*iso*metamidium) is heated with cuprous chloride–3 *N* hydrochloric acid, the theoretical quantity of nitrogen is evolved in 7–9 min., while no evolution of nitrogen occurs even after prolonged heating of the purple compound under identical conditions. Thus only the red compound contains a diazoamino-group. Recent investigations into the structure of the purple compound have revealed that it is an isomeric aminoazo compound.

As a result of this work, the formulæ provisionally suggested for the two isomers by Wragg *et al.*[1] have to be modified, and the red isomer is now shown to have structure (II) (which was originally assigned to the purple compound).

Concurrently with this investigation the original coupling reaction has been studied and conditions[2] have been established under which *iso*metamidium (II) is the main product formed, the ratio of red : purple compound being as high as 9 : 1 (polarographic determinations carried out by Dr. P. O. Kane), and the pure product is readily isolated, by standard procedures, from the reaction mixture.

The trypanocidal activity of *iso*metamidium (M. and B. 4180*A*) has been confirmed in cattle, and the results of field trials in Africa are very encouraging.

Full details of the chemical work involved in the proof of the structure of *iso*metamidium and of the modified coupling reaction will be submitted in due course to the *Journal of the Chemical Society*.

I am grateful to Dr. H. J. Barber, Dr. J. N. Ashley and colleagues of this research organization for their discussions and helpful advice.

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## 1,3-Dialkyl-6-thioxanthines : a New Series of Bronchodilators and Coronary Va odilators

1,3-Dimethylxanthine (theophylline) is readily converted into the corresponding 6-thio derivative by treatment with phosphorus pentasulphide in pyridine. The choline salt (M. and B. 4926*A*) of this derivative is more active than choline theophyllinate in relaxing the bronchial muscle (guinea pig tracheal ring preparation) and in dilating the coronary vessels (dog heart-lung preparation). This result led us to prepare and examine a series of homologous compounds, the most active in these two respects being 3-*iso*butyl-1-methyl-6-thioxanthine (M. and B. 5924).

All the thioxanthines are obtained from the corresponding xanthines in high yield by refluxing for several hours with phosphorus pentasulphide in pyridine. It was established by spectroscopic and degradation studies that thionation occurs only in the 6-position.

The choline salt of 3-*iso*butyl-1-methyl-6-thioxanthine is a pale yellow, crystalline solid, m.p. 145–147°, which is more than 50 per cent w/v soluble in water at 20°. A 10 per cent w/v solution has a *p*H of 11. Choline 6-thiotheophyllinate, m.p. 146–149°, has similar solubility characteristics.

Pharmacologically the 6-thioxanthines are very similar to theophylline, the difference in their actions being essentially quantitative. Some of the 6-thioxanthines are very much more active as bronchodilators *in vitro*, M. and B. 5924 being about sixty times as active as choline theophyllinate. *In vivo* bronchodilator activity was assessed by determining whether pretreatment would protect guinea pigs against the lethal effects of a bronchoconstrictor aerosol. The 6-thioxanthines are effective, but the relative bronchodilator activity is much less than that observed with the isolated preparation. The 3-*iso*butyl-1-methyl derivative is also more active than choline theophyllinate in dilating the coronary vessels of the dog heart-lung preparation, in dilating the coronary vessels of the anæsthetized dog and in dilating the vessels of the hind leg of the dog perfused with heparinized blood. As diuretics, however, all the thioxanthines are less potent than choline theophyllinate. Comparative results are summarized in Table 1.

Table 1. Relative Activities of Choline Theophyllinate, Choline Thiotheophyllinate and M. and B. 5924
(The activity of choline theophyllinate has been expressed arbitrarily as 1)

| Compound | Bronchodilator activity (guinea pig) | | Coronary dilator activity (dog) | Diuretic activity (rat) |
|---|---|---|---|---|
| | *In vitro* | *In vivo* | | |
| Choline theophyllinate | 1 | 1 | 1 | 1 |
| Choline thiotheophyllinate | 5 | 1 | 2–3 | < 1 |
| M. and B. 5924 | 60 | 2 | 15 | < 1 |

A full description of the chemical work will be submitted to the *Journal of the Chemical Society* and of the pharmacological work to the *British Journal of Pharmacology and Chemotherapy*.

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## Ayapin, Scopoletin and 6,7-Dimethoxycoumarin from *Dendrobium thyrsiflorum* (Reichb. f.)

During the examination of plants for phenolic constituents, the orchid *Dendrobium thyrsiflorum* was found to contain three highly fluorescent constituents (E. C. Bate-Smith, personal communication). The substances were extracted from a leaf hydrolysate with amyl alcohol and chromatographed on Whatman No. 1 paper using several different solvent systems. All the substances concerned fluoresce strongly a light blue-violet colour which is changed to green when the paper is sprayed with 2 *N* sodium hydroxide. The $R_F$ values in toluene/acetic acid/water (supernatant phase from 4 : 1 : 5 vol.) were 0·15, 0·77 and 0·85 and in 6 per cent acetic acid 0·43, 0·54 and 0·61. In Forestal solvent (hydrochloric acid/acetic acid/water) and butanol/acetic acid/water the $R_F$ values were all too high to give good separation.

The reaction with sodium hydroxide strongly resembled that given by coumarin ($R_F$ in toluene–acetic acid 0·9). The first substance, in fact, agreed in every respect with the well-known coumarin scopoletin. The other two substances, from their $R_F$ values relative to those of scopoletin and coumarin, seemed likely to be polymethoxy- or methylenedioxy-coumarins. Samples of ayapin (6,7-methylenedioxycoumarin) and 6,7-dimethoxycoumarin were therefore synthesized, and a sample of the latter and also of 5,6,7-trimethoxycoumarin were obtained from Dr. F. E. King. The dimethoxycoumarin agreed in all particulars with the second unknown substance and ayapin with the third. Trimethoxycoumarin has virtually the same $R_F$ as ayapin in toluene/acetic acid/water but its $R_F$ value in 6 per cent acetic acid is much higher (0·76), and when the paper is sprayed with alkali its fluorescence changes to bright yellow-white. The hydrolysate was chromatographed on Whatman No. 3 paper in 6 per cent acetic acid, the three substances were eluted, and their ultra-violet absorption spectra compared with synthetic standards. All showed closely similar spectra with maxima at 345 mμ and 295 mμ, a shoulder at 260 mμ and minima at 270 mμ and 305 mμ. Since the absorption spectra are quite different from other related coumarins such as herniarin, daphnetin, limetin, it is concluded that 6,7-dimethoxycoumarin and ayapin are the substances present.

In order to determine the form in which these substances occur in the plant, an extract of a leaf was made with cold methanol. This was run on Whatman No. 3 paper in 6 per cent acetic acid. No free coumarins were present, but there were three distinct fluorescent bands which were cut out and eluted. On hydrolysis the slowest-running of these gave the dimethoxycoumarin, the second gave ayapin and the third gave a mixture of these two and scopoletin. It is concluded that these coumarins occur in combination, probably as the glycosides of the corresponding *o*-coumaric acids, and that the dimethoxycoumarin and ayapin both occur in more than one glycosidic form.

I wish to thank Dr. F. E. King for the specimens of dimethoxy- and trimethoxy-coumarins and Dr. E. C. Bate-Smith for helpful advice and the facilities of his laboratory.

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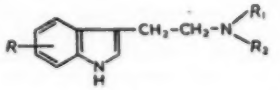
## Reserpine Analogues

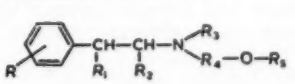
It seems likely that the most interesting pharmacological properties of the natural alkaloid reserpine are mainly determined by three chemical groups in the molecule: (1) the β-indolylethylamine group, which is present in many other natural drugs (serotonine, ergot alkaloids); (2) a tertiary nitrogen atom which is substituted by three carbon chains, one of which (the ethyl group) is attached to the indole nucleus, while the other two form part of a ring system bearing (3) a hydroxyl group which is esterified by trimethoxybenzoic acid. The β-phenylethylamine group, which is very similar to the β-indolylethylamine group, is found in another group of drugs, the adrenaline family.

On the basis of these considerations we have synthesized a number of compounds the structure of which is more or less similar to that of reserpine, in the hope that these would have useful medicinal properties. These compounds fall into two classes: β-indolylethylamine derivatives, having the general formula I:



(I)

where $R$ indicates the absence of substitution, or substitution by one or two hydroxyl or alkoxyl groups, and $R_1$ and $R_2$ are alkyl or hydroxy-alkyl groups which may be etherized or esterified; and β-phenylethylamine derivatives, II:



(II)

where $R$ indicates the absence of substitution, or substitution by one to three hydroxyl or alkoxyl

groups, $R_1$ is H or OH, $R_2$, $R_3$ and $R_4$ are H, alkyl or alkylene groups, which may be partly cyclized to give piperidyl and *cyclo*hexyl rings, as in reserpine, and $R_5$ is an alkoxybenzoyl group.

We tested all these compounds for adrenolytic and spasmolytic activity, and for their effect on the central nervous system, the heart and the circulation, with the following results.

*β-Indolylethylamine derivatives.* Some of these show properties which are very similar to those of reserpine: they potentiate hexobarbital and ether narcosis in mice, like reserpine but to a lesser extent, and show a tranquillizing effect on the same animals. Some of these compounds also have a hypotensive effect on rats and dogs, and produce bradycardia in dogs.

*β-Phenylethylamine derivatives.* Unlike reserpine, these compounds have little or no effect on the central nervous system.

Those compounds in which the phenyl group is substituted by alkoxyl groups produce spasmolysis and bradycardia; two compounds of this group, with $R = p\text{-}OCH_3$, $R_1 = H$, $R_2 = CH_3$, $R_3 = C_2H_5$, $R_4 = -(CH_2)_4-$ and $R_5$ = 3,4,5-trimethoxybenzoyl or 3,4-dimethoxybenzoyl, show a strong papaverine-like spasmolytic effect, and also atropine-like properties. The other effects are considerably weakened.

Where the phenyl group is unsubstituted or substituted by hydroxyl groups (*p*- or *m*,*p*-), on the other hand, the depressor and adrenolytic activities predominate. Two such compounds, with $R = H$, $R_1 = H$, $R_2 = H$, $R_3 = C_2H_5$, $R_4 = -(CH_2)_3-$ or $-(CH_2)_3CH-$ (with $C_2H_5$ as a branch) and $R_5$ = 3,4,5-trimethoxybenzoyl, cause a depressor effect of long duration in narcotized cats. This effect begins instantaneously and is accompanied by a slight degree of bradycardia.

Clinical investigations are in progress. The chemical synthesis of these compounds and the pharmacological investigations will be described elsewhere.

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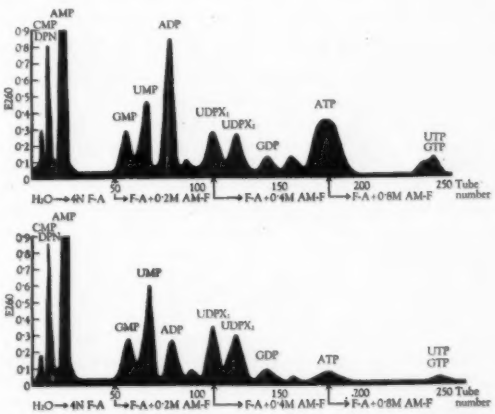
## Effects of Short-term Weaning on the Acid-soluble Ribonucleotides of Rat Mammary Gland

The physiological and biochemical changes which occur during early involution in the mammary gland are of great complexity; the gland regresses from a highly active secretory tissue to one in which the metabolic activity is greatly diminished. The ribonucleic acid and total protein content[1] has been reported to have decreased at two days of involution as does the activity of many enzyme systems[2]. Evidence is presented in this communication that marked changes occur in the acid-soluble ribonucleotides over as short a period of weaning as 12 hr.

Primiparous lactating rats of an albino strain were taken between the seventeenth to nineteenth day of lactation. The pups were removed from the mother at 9 a.m. except in experiments of 12 hr. weaning when the pups were removed at 9 p.m. Rats were killed by dislocation of the cervical vertebræ and the mammary glands were excised rapidly and put into liquid nitrogen. The acid-soluble ribonucleotides were extracted and examined by gradient elution on a 'Dowex-1' (formate form) column by essentially the method described by Hurlbert *et al.*[3].

The chromatogram obtained for the whole gland before weaning and after 12 hr. of weaning are shown in Figs. 1 and 2.




Figs. 1 and 2. Chromatograms of acid-soluble ribonucleotides extracted from the mammary gland of a late lactating rat before involution and after 12 hr. weaning, respectively. The nucleotides were eluted by the gradient elution method described by Hurlbert *et al.* (ref. 3) with three changes of solvent, as shown, from 'Dowex-1' (formate form) ion-exchange columns and collected in 5 ml. fractions. In top chromatogram the optical absorptions greater than 1·0 for adenosine monophosphate were 1·8, 1·5, 1·5 for each 5 ml. fraction; in bottom chromatogram the figures were 1·8, 2·8, 2·8, 1·8 for each 5 ml. fraction.
Abbreviations: *C*, Cytidine; *A*, adenosine; *U*, uridine; *G*, guanosine; *MP*, *DP* and *TP*, mono-, di- and tri-phosphate, respectively; $X_1$, N-acetylglucosamine; $X_2$, glucose; *DPN*, diphosphopyridine nucleotide; *F-A*, formic acid; *AM-F*, ammonium formate

On comparison of these two chromatograms it will be noticed that there is a striking decrease in the content of adenosine di- and tri-phosphates, with a correspondingly large increase in the adenosine monophosphate. This dephosphorylation seems to be general for the other nucleoside phosphates, although the uridine diphosphate complexes of acetylglucosamine and glucose are unaffected. Since the adenosine phosphates are most abundant the time course of this dephosphorylation was followed by plotting the time of weaning against the ratios of adenosine di- and tri-phosphates to adenosine monophosphate. It should be borne in mind that adenosine triphosphate is not present as a pure fraction in the chromatogram but contains other nucleotides, uridine diphosphate being the main one. This fraction at late lactation normally contains about 65 per cent adenosine triphosphate[4].

Table 1

| Animals used in experiment | Hours of weaning | Total acid-soluble ribonucleotide (μmoles/gland) |
|---|---|---|
| 2 | 0 | 16·7 |
| 1 | 2 | 14·5 |
| 1 | 4 | 10·2 |
| 1 | 6 | 10·5 |
| 1 | 8 | 15·5 |
| 2 | 12 | 13·5 |
| | Hours of lactation after 12-hr. weaning | |
| 2 | 2 | 20·5 |
| 1 | 4 | 14·7 |
| | | Mean = 14·5<br>*S.E.M.* = 1·09 |

Fig. 3 shows these ratios decrease slightly up to about the sixth hour, after which they fall rapidly to the eighth hour; from here the low values attained are constant. When lactation is restarted after 12 hr. weaning, by the re-introduction of the pups, the ratios can be seen to rise steeply, the normal lactating values being reached by 2 hr. After 4 hr. of suckling these values are still obtained. This indicates that the phenomenon is unlikely to be wholly due to diurnal variations and that even after 12 hr. weaning the dephosphorylation of adenosine di- and tri-phosphates can be reversed. Another point which emerges (see Table 1) is the constancy of the total acid-soluble ribonucleotide content of the gland throughout all the experiments undertaken. This would suggest that the catabolism of the nucleotides is not enhanced by the weaning period of 12 hr.

It has been reported by Turner[5] that weaning affects the fat composition of milk; longer periods of weaning giving rise to a lower fat content of the milk. It has been suggested that the cause is the retention by the mammary cells of fat components due to the high pressure developed in the mammary gland during weaning while the more permeable components are secreted into the alveoli of the mammary gland.

The presence of alkaline phosphatase in milk has been reported by Morton[6], and, although its function is not clearly understood, there seems little doubt that it originates in the alveolar cells of the mammary gland. It is conceivable that weaning would lead to a complete or partial retention of alkaline phosphatase in the same manner as occurs with fat under similar conditions. Such a retention would render the acid-soluble ribonucleotides vulnerable to enzymic dephosphorylation.

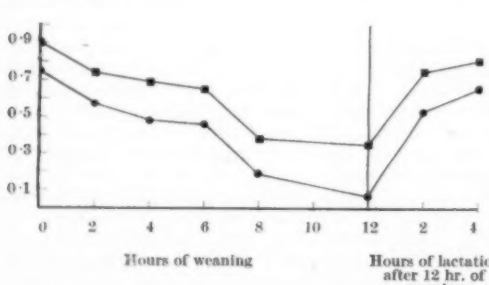



Fig. 3. Time course of dephosphorylation of adenosine polyphosphates. ■, Ratio of adenosine di- to mono-phosphate; ●, ratio of adenosine tri- to mono-phosphate

Further support for this suggestion of retention by the cell of phosphatases comes from the observed rise in pressure during weaning. Tgetgel[7] has shown that in the cow pressure in the udder increases slowly up to about the fourth hour and thereafter rapidly. Assuming a similar type of pressure curve in the rat mammary gland the drop in the ratios of adenosine triphosphate and diphosphate to monophosphate mirrors remarkably this increase.

Since adenosine di- and tri-phosphates are known to play an important part in many biosynthetic reactions which are active in the lactating mammary gland, it is possible then that the levels of the mono-, di- and tri-phosphorylated nucleosides could govern the rates of biosyntheses. Thus the rate of milk production of the rat mammary gland may be maintained by a 'feed-back' mechanism involving an increasing phosphatase activity in the cell coupled to an increasing accumulation of milk in the mammary gland.

My thanks are expressed to Drs. A. L. Greenbaum, and T. F. Slater for their guidance and helpful criticism. This work was made possible by a Medical Research Council Studentship award.

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## Reduction of α-Ketobutyrate by Human Serum

During the course of investigations into serum transaminase activities[1], it was observed that α-ketobutyrate (2-oxobutanoate) underwent enzymic reduction in the presence of serum and reduced diphosphopyridine nucleotide. At the time this was interpreted as being due to serum lactic dehydrogenase because a commercial sample of crystalline lactic dehydrogenase prepared from rabbit skeletal muscle reduced α-ketobutyrate almost as readily as its normal substrate, pyruvate[2]. Further work, however, has indicated differences between the action of serum on α-ketobutyrate and its action on pyruvate.

Dehydrogenase activities were measured spectrophotometrically at 340 mμ in 0·067 *M* Sørensen phosphate buffer at *p*H 7·4 (ref. 3). Temperature corrections were applied and all results were adjusted to 25°. The results of a typical experiment on the effect of variation of substrate concentration on the dehydrogenase activity of normal human serum is shown in Fig. 1. Maximum activity against pyruvate occurred when the substrate concentration was $0{\cdot}33 \times 10^{-3}$ *M* and at higher concentrations appreciable substrate inhibition occurred. When α-ketobutyrate was used, activity was maximal at a concentration of $3{\cdot}3 \times 10^{-3}$ *M*. The Michaelis constants calculated from these were $Km = 1{\cdot}0 \times 10^{-4}$ for pyruvate and $6{\cdot}7 \times 10^{-4}$ for α-ketobutyrate. These figures are of comparative value only since no account has been taken of the presence in serum of possible inhibitors.

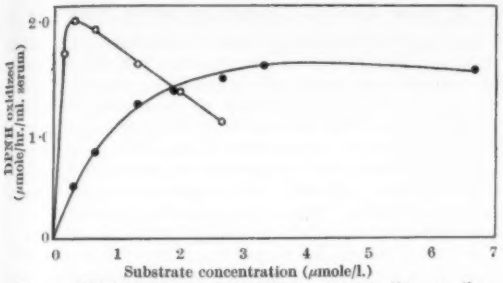


Fig. 1. Effect of changes in substrate concentration on the dehydrogenase activity of serum against pyruvate (○) and α-ketobutyrate (●)

but repetition of the experiment with other normal sera gave similar curves.

The effect of *p*H variation was measured using optimal substrate concentrations and the results appear in Fig. 2. The activity against α-ketobutyrate was maximal at *p*H 7·4 and was appreciably less at *p*H 8·0 whereas that against pyruvate was increased at the higher *p*H value.

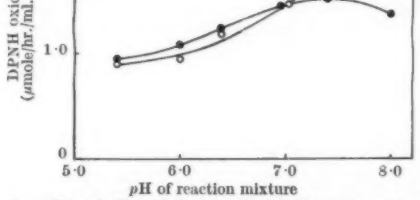


Fig. 2. Effect of *p*H variation on the dehydrogenase activity of serum against pyruvate (○) and α-ketobutyrate (●)

Over the range 21–28°, the temperature coefficient was found to be linear in both cases, but was slightly greater for pyruvate (8 per cent/deg. C.) than for α-ketobutyrate (6 per cent/deg. C.).

No inhibition of enzymic activity by a final concentration of $1{\cdot}67 \times 10^{-3}$ *M* azide, fluoride, cyanide, iodoacetate, sequestrate or oxine was observed, but $6{\cdot}67 \times 10^{-3}$ *M* cyanide reduced the activity against both substrates to a similar extent.

Four normal sera were fractionated by means of continuous paper electrophoresis using barbitone buffer of *p*H 8·6 ($\mu = 0{\cdot}05$). Lactic dehydrogenase activity was detected in the $\alpha_1$-, $\alpha_2$-, β- and γ-globulin fractions. The enzyme present in the β- and γ-globulin fractions, however, was much more active against pyruvate than against α-ketobutyrate whereas that in the α-globulin fractions showed only slightly greater activity against pyruvate (Fig. 3).

The dehydrogenase activities of a number of normal and pathological sera were examined. The ratio of the activities against pyruvate and α-ketobutyrate was found to vary between 1·4 : 1 and 1·1 to 1, figures well outside the limits of experimental error.

The differences in temperature coefficients, Michaelis constants and *p*H optima shown by serum towards the two substrates could possibly be explained by the effect of substrate variation on a single enzyme system. This is unlikely since serum lactic dehydrogenase has been shown to be electrophoretically heterogeneous[4–7], and we have demonstrated that, although each globulin fraction exhibits activity against both pyruvate and α-ketobutyrate, the relative activities in each fraction are not parallel. It is therefore suggested that this variation indicates a difference in the properties of the components of serum lactic dehydrogenase or that there exists in serum an enzyme other than lactic dehydrogenase capable of reducing α-ketobutyrate.

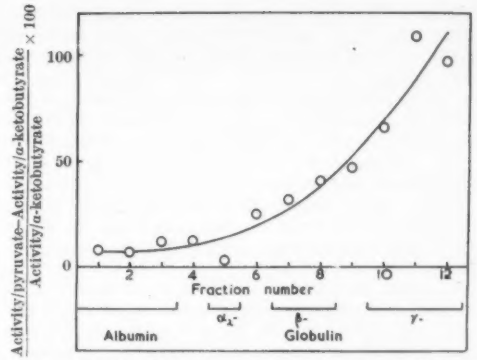


Fig. 3. Percentage differences in the dehydrogenase activity of electrophoretic fractions of human sera towards pyruvate and α-ketobutyrate. 2 ml. serum was separated into 12 fractions which were assayed separately for enzyme activity. Each point represents the mean percentage difference in the activities against these substrates exhibited by four different sera. Differences were not included when the total activity was less than 0·20 μmole/hr.

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## Composition of the Free Fatty Acid Fraction in the Plasma of Human Arterial Blood

The importance of free fatty acids as the main form in which fat is mobilized from depots and extracted by tissues has been stressed during the past few years. Several methods for their estimation in plasma are now available. One of the most widely used is that of Gordon *et al.*[1], which seems to measure the long-chain fatty acids[2] more specifically than any other. The exact composition of the fatty acids which are extracted from human plasma by this method has not, however, been determined. Their composition is of importance in metabolic studies where a knowledge of the mean molecular weight, double-bond index, and oxygen equivalent may be required.

We have analysed the free fatty acids extracted from the plasma of arterial blood by Gordon's method in eleven people who had fasted overnight. After titration, the soaps of the fatty acids in the alkaline ethanol–water phase were reconverted into free fatty acids which were methylated by means of diazo-

methane. The methyl esters were then diluted in diethyl ether and analysed in a Pye argon chromatograph. Polyvinyl acetate was used as the stationary phase, supported on 'Celite' (100–120 mesh). This stationary phase gave a separation at least as good as polyethylene glycol adipate and it had the further advantage of easier preparation and greater stability in the operating temperature (160–165° C.). The identification of the chromatograph peaks was made by using pure standards, supplemented by the method described by F. P. Woodford and C. M. Van Cent[3]. The area of each peak was measured by the triangulation procedure.

The main constituents are listed in Table 1. They are expressed as percentages of the total area of the major peaks. Oleic acid accounted for almost half. Apart from these major components, small traces of other fatty acids were found. These appeared to consist of *n*- nonanoic (pelargonic), decanoic (capric), pentadecanoic (15 : 0) and heptadecanoic (margaric) acids. Branched-chain fatty acids were also found as branched 14 : 0, 15 : 0, 16 : 0 and 18 : 0. The double-bond index[4] was 24·41 ± 3·7 (mean ± *S.D.*). The mean molecular weight was found to be 270·8, which is lower than it has previously been assumed. The mean number of oxygen molecules required for complete oxidation of one equivalent of fatty acid found during titration was calculated to be 24·32.

Table 1

| Fatty acids | | Mean (per cent) *S.D.* |
|---|---|---|
| Lauric | (12 : 0) | 0·62 ± 0·16 |
| Myristic | (14 : 0) | 3·91 ± 1·87 |
| Myristoleic | (14 : 1) | 0·70 ± 0·34 |
| Palmitic | (16 : 0) | 25·12 ± 1·51 |
| Palmitoleic | (16 : 1) | 7·52 ± 2·14 |
| Stearic | (18 : 0) | 9·43 ± 2·33 |
| Oleic | (18 : 1) | 45·54 ± 4·42 |
| Linoleic | (18 : 2) | 7·04 ± 1·59 |

The results are different from those obtained by Dole *et al.*[4], who used Dole's method of extraction[5] of free fatty acids from plasma of human venous blood. The chief difference is in the percentage of oleic acid present, which Dole *et al.* found to be 28·9 per cent, and in the double-bond index which they found to be 28.

These differences may be due to variations in the diet of the subjects studied. Theoretically they could also be due to changes which might occur between arterial and venous blood. Work which is being carried out in this laboratory, however, suggests that the changes in composition of free fatty acids during the passage of blood through a resting limb are very small. It seems likely, therefore, that the composition of the free fatty acids extracted depends on the method used.

We are grateful to Dr. S. Paul and Mr. T. D. Heyes of the Research Department, Lever Bros., Ltd., for technical advice and for providing us with pure standards of fatty acids.

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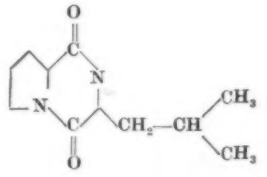
## A New Cyclic Dipeptide from Peptone

While investigating the antifungal principle derived from cultures of a *Bacillus subtilis* strain, a crystalline substance was obtained as one of the by-products. It was necessary to decide whether the crystals were a metabolite of the organism or originally contained in peptone used as a dietary essential. The same procedure succeeded in isolating the same crystals from peptone. The peptone was commercially available as 'Mikuni peptone' in Japan.

Purification was effected by recrystallization from a benzene–petroleum ether mixture. The crystals, purified as colourless needles, melted at 159·5° and was readily soluble in alcohols, chloroform and benzene and insoluble in water, ether and hydrocarbons. Carbon–hydrogen and nitrogen analysis and molecular weight measurement by Rast's method indicated molecular formulæ of $C_{11}H_{18}N_2O_2$. The infra-red spectrum showed absorption at 3,260 cm., 1,670 cm. and 1,630 cm., but no absorption of the 1,550-cm. region, which is characteristic of a cyclic amide. Significant optical rotation in methanol solution was observed as $[\alpha]_D^5 = -132·8°$. Hydrolysis with 6 *N* hydrochloric acid in a sealed tube at 110° for 20 hr. produced amino-acids. Qualitative analysis for the amino-acids by paper chromatography indicated equimolecular quantities of proline and leucine. All the results are in agreement for a cyclic dipeptide composed of two parts, proline and leucine.



It is perhaps of some interest that one of the 2,5-piperazinediones is contained in a natural substance, although certain proof of its original existence in raw meat evidently needs further investigation.

Work on the biological activity of the peptide is being carried on in several organisms.

We are grateful to Dr. Ichiji Mibuchi, Shizuoka College of Pharmacy, for discussion.

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## Stabilization of Thymidylate Kinase Activity by Thymidylate and by Thymidine

We have recently reported that an increase in thymidylate kinase activity occurs in rat liver and kidney following injection of thymidine into the intact animal[1]. Subsequent work has revealed that this enzyme activity is labile in the absence of, but stable in the presence of, thymidylate or thymidine. In this communication we wish to report the results of this work on stabilization of thymidylate kinase activity, and to consider the possible relation of these observations to the increase in kinase activity which follows thymidine administration.

Liver and thymus were removed from 200–300 gm. male Wistar rats, which were killed by decapitation. Regenerating liver was obtained from rats subjected

to 70 per cent hepatectomy[2] under ether anæsthesia 48 hr. earlier. Frozen calf thymus was obtained from commercial sources. Tissue extracts were prepared by grinding in an all-glass homogenizer 200 mgm. of acetone powder[3] with 2 ml. of ice-cold 0·1 *M tris*-(hydroxymethyl)aminomethane (*tris*) buffer, *p*H 7·5, or 1 gm. of fresh tissue with 5 ml. of buffer, followed by centrifugation at 0° for 10 min. at 10,000 r.p.m. Nucleosides and nucleotides of the highest purity commercially available were used. Thymidine and thymidylate were further purified by ion exchange and paper chromatography. Thymidylate-$^{32}$P was synthesized chemically from thymidine and $^{32}$P-orthophosphoric acid by the procedure described by Hurwitz for cytidylic acid[4] and purified by ion exchange and paper chromatography. 98 per cent of the radioactivity in the final product was hydrolysed by snake venom phosphatase and 99 per cent by semen phosphomonoesterase[5]. Thymidylate kinase activity was assayed by a slight modification of the method of Lehmann *et al.*[6]. In the first stage of the procedure three components were employed: 0·1 *M tris* buffer, *p*H 7·5 (150–195 μl.), tissue extract (5–50 μl.), and substrate mixture (100 μl.) of the following composition: 40 μmoles of *tris* buffer (0·1 *M*, *p*H 7·5), 4 μmoles of magnesium chloride, 2 μmoles of adenosine triphosphate and 40 mμmoles of thymidylate-$^{32}$P containing 50–200 c.p.m./mμmole. The sequence of addition of each component was found to be important (see below), and for maximum enzyme activity the reaction was started by adding tissue extract as the last component. The reaction mixture was incubated for 15 or 30 min. at 37°, and the reaction was stopped by heating in a boiling water-bath for 2 min. In the second stage the unreacted thymidylate was hydrolysed with semen phosphomonoesterase as described[6]. Finally, the phosphomonoesterase-resistant material was adsorbed on charcoal, which, in turn, was collected on a membrane filter ('Ultraflex', Schleicher and Schuell Co.), washed thoroughly with cold water, dried, and counted with a micromil end-window counter. All values were corrected for a blank containing no enzyme. A unit of enzyme activity is defined as that amount of enzyme which in 1 hr. renders 100 mμmoles of thymidylate resistant to phosphomonoesterase. The specific activity is expressed as units per mgm. of protein, determined by the method of Lowry *et al.*[7].

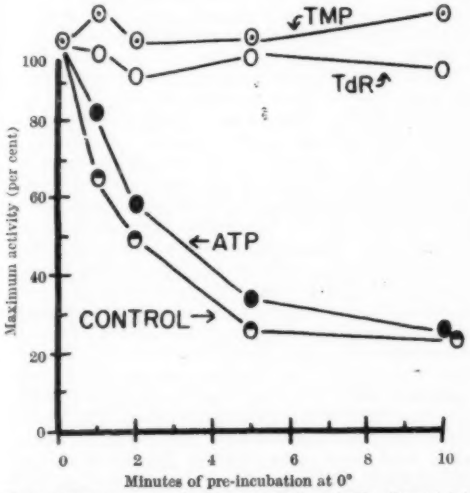


Fig. 1. Effect of pre-incubation at 0° with *tris* buffer, thymidylate (TMP), adenosine triphosphate (ATP) and thymidine (TdR) on thymidylate kinase activity. 5 μl. (200 μgm. protein) of an extract of 48-hr. regenerating rat liver acetone powder was pre-incubated at 0° with 195 μl. of *tris* buffer alone ('control'), or with buffer containing 1 mμmole of thymidylate, 10 mμmoles of thymidine, or 10 mμmoles of adenosine triphosphate in a final volume of 200 μl. At the intervals indicated, enzyme activity was determined by adding 100 μl. of substrate mixture (cf. text) and incubating at 37° for 30 min. The results are expressed as percentage of maximum enzyme activity, determined by assaying the extract without pre-incubation

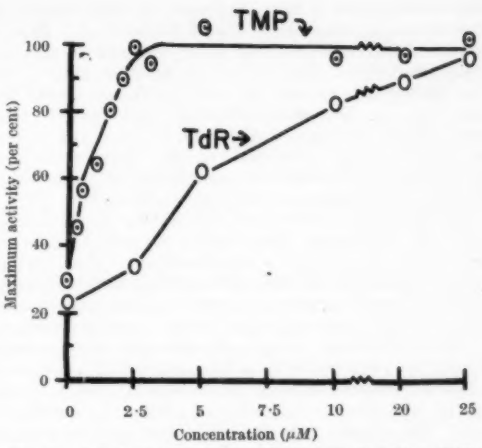


Fig. 2. Effect of thymidylate (TMP) and thymidine (TdR) concentration on thymidylate kinase activity during pre-incubation at 0°. Tissue extract (as in Fig. 1) was pre-incubated at 0° for 10 min. with 195 μl. of *tris* buffer containing the indicated amounts of thymidylate or thymidine. The activity was assayed and the results expressed as in Fig. 1

'Pre-incubation' of tissue extract in *tris* buffer at 0° prior to incubation at 37° with the substrate mixture resulted in a rapid, irreversible decrease of enzyme activity to a minimal value of 20 per cent (curve marked 'control' in Fig. 1) of that found in the same extract assayed without pre-incubation. This observation suggested that a substance in the substrate mixture was protecting the enzyme against loss of activity. Hence, adenosine triphosphate and thymidylate were added separately to the buffer in which the tissue extract was diluted and pre-incubated. Enzyme activity was protected fully when thymidylate was present in the diluent (curve marked TMP in Fig. 1), but adenosine triphosphate had no effect. Thymidine also protected enzyme activity (Fig. 1), but for full protection 10 times as much thymidine (25 μ*M*) was required as compared with thymidylate (Fig. 2). The following compounds at concentrations of 2·5 μ*M* and 25 μ*M* did not protect thymidylate kinase activity in the dilution test: the monophosphates of adenosine, guanosine, cytidine and uridine, and the corresponding deoxyribonucleotides; cytidine, uridine, deoxycytidine, deoxyuridine, and thymine. Bovine serum albumin, ribonucleic acid and deoxyribonucleic acid were also without effect. The supernatant solution obtained by boiling

liver extract for 2 min. followed by centrifugation protected the enzyme in the dilution test. Boiled extract from regenerating liver exerted a greater protective effect than did that from resting liver. The protective factor in boiled extract could be adsorbed on activated charcoal and eluted with ammoniated ethanol. Although it has yet to be identified, it is presumed to be thymidylate or thymidine in view of the specificity of these compounds with respect to enzyme stabilization.

The inclusion of 10 m*M* thymidine in the buffer used for extracting fresh tissue or acetone powder has resulted not only in stabilization of thymidylate kinase activity in the dilution test, but also in a larger yield of enzyme activity (Table 1). This observation has proved of practical value in our present efforts to purify the enzyme. With preparations from regenerating rat liver full recovery of kinase activity is achieved following dialysis against thymidine at *p*H 7·5, but in the absence of thymidine activity is completely lost. This is also true for other manipulations, such as salt fractionation and gel adsorption.

Table 1. Effect of Thymidine in the Extraction Medium on Thymidylate Kinase Activity

| Preparation | Extraction medium | Thymidylate kinase activity (units/mgm. protein × $10^3$) | |
|---|---|---|---|
| | | Control | Pre-incubated for 10 min. |
| 48-hr. regenerating rat liver acetone powder extract (5 μl.; 200 μgm. protein) | *Tris* buffer | 26·9 | 6·1 |
| | 10 m*M* thymidine in *tris* buffer | 32·1 | 30·9 |
| Resting rat liver extract (50 μl.; 900 μgm. protein) | *Tris* buffer | 1·3 | 0·7 |
| | 10 m*M* thymidine in *tris* buffer | 2·4 | 2·7 |
| Rat thymus extract (20 μl.; 140 μgm. protein) | *Tris* buffer | 74·2 | 15·7 |
| | 10 m*M* thymidine in *tris* buffer | 132·0 | 144·0 |
| Frozen calf thymus acetone powder extract (5 μl.; 100 μgm. protein) | *Tris* buffer | 84·0 | 22·0 |
| | 10 m*M* thymidine in *tris* buffer | 117·0 | 120·0 |

The demonstration that thymidylate kinase activity is labile under certain conditions, but is stabilized by thymidylate and by thymidine, suggests that the increase in enzyme activity in rat tissues following *in vivo* thymidine administration is at least in part attributable to protection of the enzyme by its substrate. Work now in progress with purified enzyme preparations is designed to test this hypothesis and to elucidate the mechanism of enzyme protection by thymidine and by thymidylate.

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## PHYSIOLOGY

### Specificity of the Effects of Cardiac Glycosides on the Rhythmic Contraction of Single Cultured Cardiac Muscle Cells

From fragments of embryonic chick hearts treated with trypsin, single, rhythmically contracting cells can be grown in a fluid, semisynthetic culture medium[1]. Exposure of these cells to cardiac glycosides in concentrations as low as $10^{-9}$–$10^{-8}$ *M* results in an increase in the rate of beat[2]. In addition the pulsations appear to become stronger. At concentrations of $10^{-7}$ *M* and above, the acceleration of pulsation is soon followed, or is accompanied, by disturbances of automaticity and of co-ordinated contractile activity. By means of phase-contrast, high-speed microcinematography of cells anchored to the glass surface these effects could be studied in greater detail[3]. The motion pictures revealed changes at the cellular level which strikingly resembled some of the familiar manifestations of digitalis poisoning in the heart of animals and of man. Such phenomena as partial and complete block of propagation of the contraction wave (presumably due to block of conduction), bigeminal rhythm, ectopic beats, tachycardia, and fibrillation could all be observed in single isolated ventricle cells.

It seemed worth while to find out whether these effects were specific in the sense that they are elicited solely or preferentially by compounds possessing the various molecular features required for the characteristic action of the cardiac glycosides on the intact heart. By the use of compounds lacking one or the other of these features, but possessing the rest of them, it has been possible to establish a fairly high degree of structure-dependent specificity for the action of cardiac glycosides on cation movement in erythrocytes[4] and on respiratory cardiac tissue metabolism[5], and to rule out such specificity for certain effects exerted on contractile heart muscle proteins[6].

Two compounds of this type, hexahydroscillaren *A* and allocymarin, were selected for the experiments described below. They were compared to the closely related, biologically potent natural glycosides, scillaren *A* and cymarin. Hexahydroscillaren *A* is derived from scillaren *A* by hydrogenation of the doubly unsaturated six-membered lactone side grouping and of the 4,5-double bond in the steroid nucleus, the $C_5$-hydrogen atom assuming the α-orientation (*trans* junction of rings *A* and *B*). Allocymarin (17-*iso*cymarin) is formed from cymarin by inversion of the substituents at $C_{17}$ of the nucleus, the butenolide ring becoming α-oriented. Except for an antagonism exhibited under certain conditions against scillaren *A*, hexahydroscillaren *A* has no significant effect on the heart, while the potency of allocymarin is about 1/100 that of cymarin[7]. Solutions of the glycosides in ethanol (5 mgm./ml.) were prepared and were appropriately diluted with culture medium prior to use.

Single pulsating myoblasts were grown under sterile conditions in sealed and inverted hollow-ground slides by the method referred to above from enzymatically and mechanically dissociated ventricular cardiac muscle of 13 days old chick embryos. After 24 hr. of incubation at 37° C. the initially spherically shaped cells had flattened on, and become fastened to, the surface of the cover slip. The culture

Table 1. Comparison of the Effects of Hexahydroscillaren *A* and Scillaren *A* and of Allocymarin and Cymarin on Isolated Pulsating Myoblasts cultured from Embryonic Chick Heart Ventricles

| Culture No. | Glycoside | Concentration | | Number of cells observed | Rate of pulsation, Mean ± standard deviation | *P* | Irregularities of pulsation |
|---|---|---|---|---|---|---|---|
| | | μgm./ml. | μmoles/l. | | | | |
| 7 | — | — | — | 44 | 52 ± 17 | | No |
| 7 | Hexahydroscillaren *A* | 1·0 | 1·43 | 50 | 57 ± 17 | ~ 0·25 | No |
| 7 | — | — | — | 22 | 55 ± 16 | | No |
| 7 | Scillaren *A* | 0·1 | 0·14 | 13 | 84 ± 35 | < 0·005 | Yes |
| 1 | — | — | — | 22 | 52 ± 21 | | No |
| 1 | Allocymarin | 1·0 | 1·82 | 48 | 57 ± 20 | ~ 0·5 | No |
| 8 | — | — | — | 45 | 54 ± 28 | | No |
| 8 | Cymarin | 0·1 | 0·18 | 87 | 72 ± 34 | < 0·005 | Yes |

medium was then changed several times in order to ascertain that the rate of pulsation was not affected by fresh medium. A final change was made to medium containing glycoside or ethanol, the concentration of the latter corresponding to that of the alcohol in the glycoside solution (0·002 and 0·02 per cent). The cells were observed at 37 ± 0·3° C. with a phase-contrast microscope equipped with a warm stage.

Table 1 summarizes the results of experiments in which scillaren *A* and cymarin were used in final concentrations of $1 \cdot 4$ and $1 \cdot 8 \times 10^{-7}$ *M*, respectively, while the concentration of their structural analogues was set at $1 \cdot 4$ and $1 \cdot 8 \times 10^{-6}$ *M*. The results show that scillaren *A* and cymarin caused a significant increase in the rate of pulsation. They also caused previously quiescent cells to pulsate. In a number of cells disturbances of rhythm and contraction were observed, terminating in some instances in fibrillatory movements and stand-still. Hexahydroscillaren *A* and allocymarin on the other hand, though present at ten times higher concentrations than their cardio-active congeners, were without significant chronotropic action, did not induce rhythmicity in quiescent cells, and produced no irregularities of beat. Thus the structural requirements for the display of biological activity by steroid lactones are as stringent in the cultured embryonic heart cell, at least so far as the present structure–activity relationships are concerned, as they are known to be in the adult vertebrate heart.

These findings make us feel rather confident that in our previous work on the behaviour of cultured heart muscle cells in the presence of cardiac glycosides we had not been dealing with irrelevant phenomena. One is encouraged to pursue the study further of this variety of a cardiac cell for whatever new information it might yield on the cellular basis of cardiac glycoside action.

We are indebted to Prof. A. Stoll, Basle, for a gift of hexahydroscillaren *A* and scillaren *A* and to Prof. T. Reichstein, Basle, for a gift of allocymarin and cymarin.

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## Adrenaline and Blood Lipids

Adrenaline has a powerful effect on carbohydrate metabolism. The effect of this hormone on nitrogen excretion has also been studied[1]. However, little is known about its effect on blood lipids. In the present work, adrenaline was administered in doses of 1 mgm. to normal individuals after a 14-hr. fasting period. Blood samples were taken initially and every hour for 4 hr. after the injection. In all samples total lipids and phospholipid phosphorus were measured. For the determination of total fats the following method was used[2]: 0·1 ml. of plasma was applied to a filter paper and dried. The filter paper was previously washed with alcohol/ether solution 3 : 1. The paper with the dried plasma was soaked for 60 min. in a sudan black solution (100 mgm. of the dye in 100 ml. of 50 per cent ethanol) and then washed three times for 15 min. with 50 per cent ethanol. The spots were cut and eluted in 6 ml. of 25 per cent acetic acid in ethanol. The colour density was determined at 590 μm. The results are expressed in mgm. of lipids per 100 ml. A calibration curve was prepared by using a standard solution of purified olive oil (1 per cent in a hot mixture of alcohol/ether 3 : 1). It was noticed from preliminary experiments that by this method nearly all lipids are measured. This method is more sensitive for determination of plasma lipids than visible lipæmia, and proved satisfactory for routine work.

For determination of phospholipids the Zilversnit–Davis method was used[3]. The results are expressed in mgm. of phospholipid phosphorus per cent.

The effect of adrenaline on plasma lipids is presented in Table 1. Normal untreated individuals show a trend towards an increase in total lipids in plasma, due probably to mobilization of depot fats. The phospholipid phosphorus remains practically constant. Individuals treated with adrenaline showed a slight decrease in total lipids accompanied by an increase in phospholipid phosphorus.

Table 1. Effect of Adrenaline on Plasma Lipids

| | Control | | | Adrenaline | | |
|---|---|---|---|---|---|---|
| | *T.L.* | *P.P.* | *R.* | *T.L.* | *P.P.* | *R.* |
| Before injection | 307 ± 13·7 | 9·85 ± 0·22 | 3·17 | 312 ± 11·2 | 9·75 ± 0·31 | 3·12 |
| First hour | 317 ± 11·3 | 9·25 ± 0·29 | 2·93 | 300 ± 5·6 | 10·30 ± 0·09 | 3·43 |
| Second hour | 320 ± 9·4 | 9·30 ± 0·24 | 2·90 | 302 ± 4·1 | 11·90 ± 0·08* | 3·94 |
| Third hour | 332 ± 6·3 | 9·50 ± 0·19 | 2·90 | 307 ± 8·2 | 12·70 ± 0·18* | 4·09 |
| Fourth hour | 340 ± 7·2 | 10·00 ± 0·20 | 2·94 | 305 ± 9·3 | 10·40 ± 0·25 | 3·49 |

*T.L.*, Total lipids (mgm. per cent); *P.P.*, phospholipid phosphorus (mgm. per cent); *R*, ratio *P.P./T.L.* The values represent the average of 18 individuals, after a 14-hr. fasting period. Adrenaline was given, 1 mgm. subcutaneously.
* $P < 0 \cdot 02$.

The effect of adrenaline on plasma is better illustrated by calculating the ratio phospholipid phosphorus/total lipid. There is a definite increase in this ratio after administration of adrenaline, which is evident after the first post-injection hour and lasts 1–3 hr.

That adrenaline may have an effect on lipid metabolism is suggested by the observation that large doses of adrenaline (1 mgm. per kgm. body-weight) in rabbits produce a calorigenic effect, 2–3 hr. after injection, along with a decrease in plasma fatty acids[4]. However, this experiment gives no information on phospholipid phosphorus, and the doses used do not approach any physiological or therapeutic dose. From our experiment the conclusion is drawn that adrenaline increases the percentage of phospholipid component of serum lipids.

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## Catalase Activity of Mouse Liver and its Relation to the Condition of the Animal

In papers dealing with methods of determining catalase activity in animal tissue, while dealing with the experimental conditions, usually little attention is paid to the condition of the animal. We have found the latter to be of utmost importance.

The two methods mostly employed in the determination of catalase activity in animal tissue, the titrimetric and gasometric method, have been compared by Greenstein[1] and by Dounce and Shanewise[2]. The former found different values; the latter workers obtained the same values in both methods. Chance[3] made a thorough spectrophotometric investigation of the decomposition of hydrogen peroxide by catalase.

In our experiments we used the apparatus described by Appleman[4]. The animal was killed by decapitation, the liver removed, weighed and homogenized with 3 ml. water in a Griffith tube. After centrifugation the supernatant was diluted with 0·1 *N* Sörensen phosphate buffer of *p*H 7·0. 3 ml. of this solution—equivalent to about 0·9 mgm. of tissue—were mixed in the Appleman apparatus with 5 ml. of 3 per cent hydrogen peroxide buffered with 0·1 *N* Sörensen phosphate buffer solution at 29° C. The unit of catalase activity (activity factor) is expressed as ml. oxygen per gram tissue (dotted lines in Fig. 1) or per whole liver (solid lines in Fig. 1) per second. The reproducibility was better than 5 per cent.

We used male homozygotic Swiss mice in order to exclude possible differences in liver catalase activity of the two sexes as reported by Adams[5].

We expected a normal distribution curve (symmetrically, positively or negatively J-shaped) of the activity factors of normal mice. Curve I was obtained (dotted lines, activity factors per gram; solid lines, per whole liver).

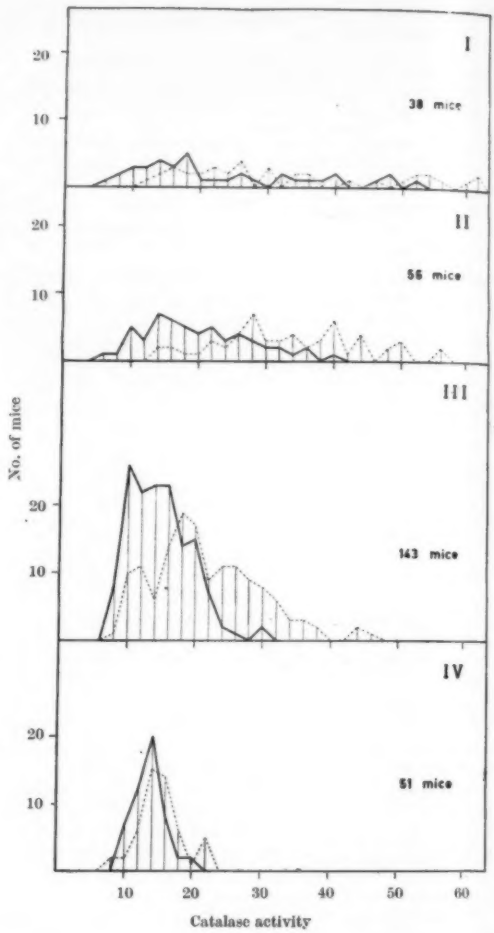


Fig. 1

Fasting the mice for 24 hr. before the analysis gave a slightly better picture (curve II).

We then reasoned that placing the animal in a 'steady state' probably would give better results. We imagined the liver to be composed of machinery (enzyme systems) and products (glycogen, proteins). When all mice receive the same food (quality and quantity) and have to produce the same amount of energy every day, one would expect that the liver would be in a 'steady state', and therefore the enzyme apparatus in all the mice livers would be practically the same. For the determination of liver catalase in this way we used mice 38–57 days old, which we raised in a stable at 24° C. They were exposed to artificial light from 8.30 until 17.00 hr. Every mouse of the same age received the same quantity and quality of food. Water was given *ad libitum*. The results are reproduced in curve III.

During cold nights the stable did not reach 24° C., so finally we set up an experiment using constant temperatures in the stable. Only normal growing mice—controlled by weighing—were used. All organs of the mice used were checked macroscopically for abnormalities; if any were found, the respective

activity factor was excluded. All mice were adult (about 90 days old). The result is shown in curve IV. The spread in liver catalase activity factors per whole liver was thus reduced from 4–54 (curve I) to 8–22 (curve IV) or to 28 per cent of the original value.

With this method we tested substances separated from cancer tissue. When injected in mice the substances produce a marked decrease in liver catalase activity. Our results agree with those of Nakahara and Fukuoka with 'toxohormone'[6].

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## Toxicity of a Single Subcutaneous Dose of Sodium Selenite in Pigs

SINCE the activity of 'factor 3' in liver necrosis in rats and exudative diathesis in chicks was shown to be dependent on selenium[1], compounds of this element have been shown to prevent other diseases induced by tocopherol-deficient diets. Sodium selenite (0·2 p.p.m.) as well as tocopherol acetate inhibit muscular degeneration in pigs fed grain, which causes field outbreaks[2]. Muscular degeneration in pigs is associated with a rise in plasma glutamic-oxaloacetic transaminase, but normal ornithine-carbamyl transferase[3]. When the disease is manifested, high glutamic-oxaloacetic transaminase levels rapidly return to normal after subcutaneous administration of 0·02 mgm. selenium (as $Na_2SeO_3$) per kgm. body-weight daily for three days (Orstadius *et al.*, unpublished work).

In veterinary medicine selenium has long since been known as a cause of poisoning in farm animals ('blind staggers', 'alkali disease'). 6–8 mgm. selenium per pound of body-weight as a single oral dose of sodium selenite is the minimum lethal dose for pigs[4]. Intoxicated animals showed emesis, diarrhœa, apathy, unwillingness to move, shivering and sometimes paresis before death. No thorough examination of the muscles was done.

Sodium selenite was given subcutaneously to pigs weighing 30–70 kgm. 2·0 mgm. and 1·2 mgm. selenium per kgm. body-weight caused death after 4 hr. and five days, respectively, during which time the pigs showed trembling, ataxia and paresis. Plasma glutamic-oxaloacetic transaminase was significantly increased (Fig. 1); but plasma ornithine-carbamyl transferase was normal, indicating that muscle but not the liver was affected[3]. At post-mortem examination the body musculature showed extensive dystrophy; but other organs, including the liver, showed no significant changes.

0·9–1·1 mgm. selenium per kgm. body-weight caused slight to moderate elevation of plasma glutamic-oxaloacetic transaminase in about half the number of pigs so treated, but otherwise no symptoms of disease. The ornithine-carbamyl transferase values were normal. The elevations of glutamic-oxaloacetic transaminase returned to the starting-level after a day or two. Biopsy specimens from the longissimus dorsi showed no changes at microscopical examination.

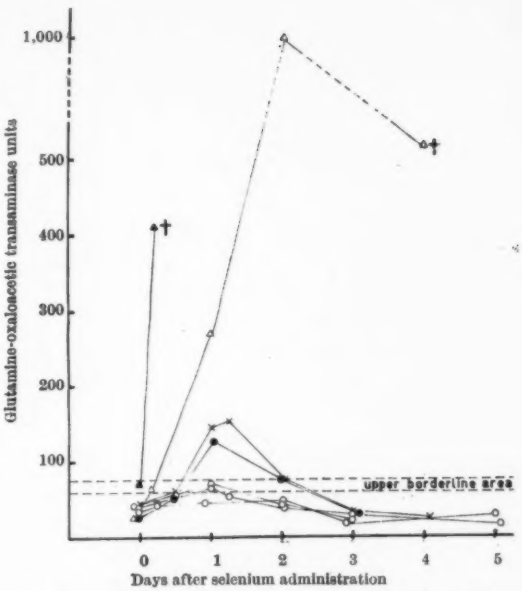


Fig. 1. ×, 0·9; ○, 1·0; ●, 1·1; △, 1·2; ▲, 2·0 mgm./kgm. body-weight

0·8 mgm. selenium per kgm. body-weight or smaller doses gave no increase of transaminase.

It is remarkable that the anti-muscular degeneration effect of low selenium doses corresponds to a high vulnerability of the muscles to increased selenium doses.

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## Effects of γ-Aminobutyric Acid and Picrotoxin on Spontaneous Activity in the Central Nervous System of the Crayfish

SINCE the extraction of an inhibitory substance (factor I) from mammalian brain[1], one constituent of which was identified as γ-aminobutyric acid[2], this constituent has been tried on a number of invertebrate preparations[3]. It imitates the action of inhibitory neurones in crayfish and on injection into the animal results in flaccidity[3]. The action of γ-aminobutyric acid is very similar to that obtained on stimulation of the inhibitory fibres in crayfish stretch receptors[4]. The effects of γ-aminobutyric acid are counteracted by picrotoxin in this preparation[3] as well as in crayfish hearts[5]. Picrotoxin

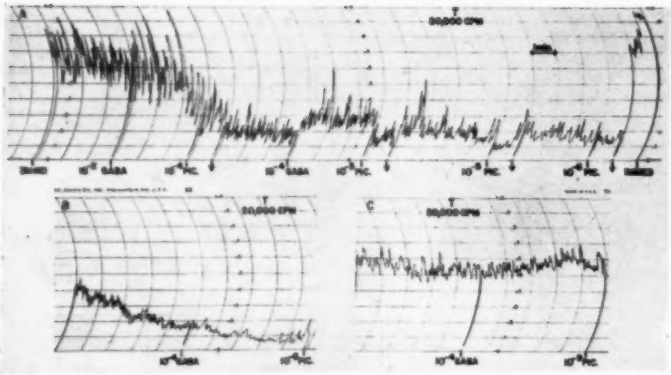

Fig. 1. Records of integrated electrical activity in 3-γ-aminobutyric acid-picrotoxin antagonism experiments. Records should be read from right to left. Full scale is 20,000 impulses per min.; vertical lines delineate 1 min. periods of recording; arrows indicate periods of rinsing in van Harreveld's solution; *'IMMED'* shows activity recorded immediately after isolation of the ganglion. *A*, *p*H 7·5; *B*, *p*H 6·6; *C*, picrotoxin *p*H 7·5, γ-aminobutyric acid *p*H 6·6

by itself is a convulsant in crayfish[6,7] although no effect on synaptic transmission is observed using $2{\cdot}5 \times 10^{-4}$ *M* picrotoxin[8]. However, concentrations greater than $10^{-6}$ *M* progressively decrease the effect of inhibitory nerve stimulation in crayfish claws[9].

Although only peripheral inhibition has been demonstrated in the crayfish, it is not unreasonable to expect that inhibitory pathways may be present in the central nervous system. If this is so, it might be possible to demonstrate them if the transmission process is blocked by picrotoxin and depends on γ-aminobutyric acid.

The preparation used was the fifth abdominal ganglion of the crayfish, *Orconectes virilis*. The ganglion was held between electrodes and the electrical activity counted by electronic scalers, integrated and then fed into a graphic ammeter. (The details of the technique used are in the thesis, "Spontaneous Electrical Activity in the Crayfish Central Nervous System", by J. K. Hichar, Harvard University, 1958, *J. Cell. Comp. Physiol.*, 55, 195; 1960). Control-levels of activity were obtained by recording the activity from the ganglion in a layer of oil after it had been immersed in a van Harreveld's solution[10] for a period of at least 15 min. After the control-level was established the ganglion was then immersed in a test solution for 1 min. and the activity recorded again after raising into the oil layer. For each level of activity obtained after contact with a drug, the preceding activity was used as the control. Normally, when the effects of a particular drug were being tested, the progression of concentrations was from weak to strong concentrations. All drug solutions were made up in van Harreveld's solution and the experiments were conducted at room temperature, which varied from 24° to 26° C.

In 4 out of 5 experiments γ-aminobutyric acid, in concentrations of $10^{-10}$ to $10^{-2}$ *M*, had no effect on spontaneous activity of the fifth ganglion; β-alanine was found to have effects similar to those of γ-aminobutyric acid on the crayfish stretch receptor but to be 1/20 as active[8]. On the ganglion β-alanine caused a gradual enhancement of the activity, commencing at $10^{-4}$ *M* and inhibition occurring at $10^{-2}$ *M*.

The effects of picrotoxin were more striking. As the concentration increased from $10^{-6}$ *M* there was a gradual increase in activity until $10^{-4}$ *M* was reached, when the activity was maximal. After exposure to $10^{-4}$ *M* picrotoxin for approximately 3 min. depression occurred. This was more obvious when yet higher concentrations were used. It was common for units to fire repetitively when treated with picrotoxin. These bursts began long before increases in overall level of activity were apparent; in most cases before a concentration of $10^{-7}$ *M* was reached. These effects were irreversible after periods of washing as long as 30 min.

Several experiments were then conducted in order to determine whether pre-treatment with picrotoxin and the resulting excitation could be influenced by subsequent treatment with γ-aminobutyric acid. The results of one such experiment appear in Fig. 1*A*. In this experiment after the usual picrotoxin excitation subsequent treatment with $10^{-4}$ or $10^{-2}$ *M* concentrations of γ-aminobutyric acid failed to influence this high level of activity.

To determine if a lower *p*H would change the activity in any way, as was suggested by Florey[1], a nerve cord was soaked in $10^{-2}$ *M* picrotoxin for 30 min. at a *p*H of 6·6. The activity was recorded for 5 min., after which the preparation was immersed in $10^{-4}$ *M* γ-aminobutyric acid of the same *p*H for 2 min. The electrical activity was again recorded for 5 min. and the results appear in Fig. 1*B*. Here it can be seen that the increase which began after the treatment with picrotoxin continued at close to the same rate after immersion in γ-aminobutyric acid.

Other experiments were conducted where nerve cords were soaked for 30 min. in $10^{-3}$ *M* picrotoxin at *p*H 7·5. Activity was recorded for 5 min. which was followed by immersion in $10^{-4}$ *M* γ-aminobutyric acid at *p*H 6·6 for 2 min. and recording again done. Results of this experiment appear in Fig. 1*C*. Here it can be seen that the initial increase in activity after soaking for 30 min. in the picrotoxin solution was in no way influenced by the considerably higher concentration of γ-aminobutyric acid, and the level remained constant.

The suggestion was made that acetylcholine and factor I are the transmitters of opposite action in crayfish[5,11]. Since no evidence was obtained for a neurohumoral function of γ-aminobutyric acid in the preparations used here, it appears that the situation may not be so simple. It may be that γ-aminobutyric acid is a precursor of factor I[12]. On the other hand, there is no *a priori* reason to assume that in an inhibitory pathway (or in any pathway for that matter) the same transmitter must be used at all synaptic junctions. It is entirely possible as in the vertebrate autonomic system that different transmitters are involved. Thus γ-aminobutyric acid might be the inhibitory transmitter at the periphery, and not be utilized in the central nervous system. However, a few experiments done on an intact animal where γ-aminobutyric acid was injected into a walking leg and proprioceptive responses were elicited from a sensory neurone, did not give evidence of any effect of the substance, although it was found to block the lobster seventh median thoracic stretch

receptor, which has no inhibitory synapse[12]. This would suggest that γ-aminobutyric acid or a substance similar to it is not a general peripheral inhibitory transmitter.

The different effects of β-alanine at central synapses found here and peripheral ones[3] suggest a central inhibitory transmitter that differs from that at the periphery. The different effects of picrotoxin observed in these two areas also support this hypothesis. The results presented here show picrotoxin to be highly irreversible in the crayfish central nervous system, whereas it appears to be easily reversible at the periphery[7,9]. Picrotoxin in low concentrations does not alter the spontaneous activity of the stretch receptor neurone, but it antagonizes the inhibitory effect of factor I[7]. Van der Kloot *et al.*[9] reported that picrotoxin blocks the effect of stimulation of the inhibitory nerve in crayfish chela muscle. Elliott and Florey[7] also reported that picrotoxin had convulsive effects in crayfish and it was found to excite the ganglia. Thus the effect of picrotoxin differs peripherally and centrally. These observations indicate that the drug may have a different action at central synapses from that at peripheral ones where the transmitters involved may differ. That is, picrotoxin may, as van der Kloot *et al.*[9] suggest, block the action of the inhibitory transmitter peripherally in a curare-like manner by joining the receptor molecule. Its central action, however, may be quite different.

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## Incorporation of Amino-Acids labelled with Carbon-14 in Nerve Proteins during Activity and Recovery

THAT nerve proteins may take an active role during nerve impulse propagation has been proposed in many publications[1]. In a paper, now in the press, I have suggested that a small fraction of the nerve proteins may split, probably to the level of amino-acids, during nerve activity, and that this process should be fully reversible, appearing as an increased turnover of proteins during impulse conduction or shortly afterwards. The purpose of the present communication is to present evidence in support of these suggestions.

In each experiment, 4–6 desheathed sciatic nerves (800–1,600 mgm. of nerve) from the South American frog *Callyptocephalus gally* were immersed for 1 hr. in 10 c.c. of Ringer solution containing 20–40 μc. of a mixture of amino-acids labelled with carbon-14 (hydrolysate of *Chlorella* protein). Then half the nerves were placed on electrodes and stimulated for 30 min. with square pulses of 0·2 msec. duration at 1–2 V. at a frequency of 120/sec. To control conduction and the maximal response, the activity of the nerves was continuously displayed on an oscilloscope. The other half of the nerves were also placed on electrodes for the same length of time, but were not stimulated. At the end of the 30 min. period, both groups were washed twice, for 15 min. each time, in Ringer solution without amino-acids. After washing, the nerves were frozen and crushed with ground glass in a mortar, and their proteins extracted in 0·1 *M* potassium chloride (15 c.c. of extract). The extracts were clarified in a refrigerated centrifuge at 20,000*g* for 1 hr. and the supernatant of each sample was treated with the same volume of 20 per cent trichloracetic acid and left overnight. Next day, the precipitates were filtered and washed with 5 per cent trichloracetic acid and with alcohol–ether (three times each). The precipitates were retained in filter papers, which were then transferred to aluminium planchets and the radioactivity of the precipitated protein was measured with a gas-flow counter (Nuclear Chicago Model *D* 47 with micromil window). Afterwards, the nitrogen content of each filter paper and precipitate was determined by micro-Kjeldahl analysis. The nitrogen content of the protein was obtained by subtracting the average nitrogen content of the filter paper.

Amino-acid incorporation of the experimental (stimulated) and control (not stimulated) samples was compared from their specific activities expressed in terms of counts/min./mgm. of nitrogen. Table 1 shows the results of seven experiments. It can be seen that the proteins from the stimulated nerves incorporated more activity than those of the controls. The average increase in activity due to stimulation was 48 per cent with a high standard deviation of 23.

Table 1

| Exp. No. | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| $E\left(\frac{\text{counts/min.}}{\text{mgm. N}}\right)$ | 136 | 151 | 118 | 135 | 175 | 185 | 139 |

$E$ = standardized specific activity of the experimental group, taking the value for the control group as 100.

These results can probably be interpreted as due to an increase in protein turnover during nerve impulse propagation or shortly afterwards. Similar observations have been made with respect to the protein turnover in the central nervous system after intense stimulation[2] (although in this latter case glucose labelled with carbon-14 was used as the source of markers). However, as the results presented here were obtained on isolated peripheral nerves, they support more directly the idea that nerve proteins have a more active role in impulse propagation and recovery than those obtained using the central nervous system, where other processes may be involved. Furthermore, these findings suggest a way of labelling the proteins that participate actively in nerve function (impulse propagation) and make possible their isolation and study.

I am indebted to Miss Ines Hoppe and Miss Silvia Rissetti for technical assistance, as well as to Miss

Emmy Wittig, who kindly carried out the nitrogen analyses. The experiments were made with equipment purchased by the Rockefeller Foundation, to which we are much in debt. I thank also Dr. Hodgson, who provided the mixture of labelled amino-acids.

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## Hydroxyproline and the Shrinkage Temperature of Collagen

Dr. B. J. Rigby and Dr. J. D. Spikes[1] have quoted a value of 8·3 per cent for the hydroxyproline content of fibrinoid tissue as being taken from a paper by Bowes, Elliott and Moss[2]. The figure given in this paper is in fact 7·6 for the hydroxyproline-nitrogen expressed as per cent of the total nitrogen of the gelatin solution obtained on autoclaving fibrinoid tissue. Assuming a total nitrogen content of 18 per cent, this corresponds to 12·8 per cent hydroxyproline on protein weight which, according to Fig. 1 of Rigby and Spikes, should give a $T_s$ of 60° or more. Their suggestion that rheumatic effects are the result of a structural breakdown due to temperature effects only is, therefore, not supported.

We would also like to direct the attention of the authors to certain exceptions to the argument that the $T_s$ of collagen is related to its hydroxyproline content, for example, invertebrate collagens[3–5].

In the absence of any evidence that the preparation is homogeneous it seems more likely that variation in the hydroxyproline content of mammalian tissues is an indication of the collagen content, rather than of differences in the composition of the collagen itself.

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WE regret the error in our original publication[1], and thank Drs. Bowes and Moss for the correction. As they point out, the $T_s$ corresponding to the correct value for the hydroxyproline in the example quoted is about 60° C. However, as was stated in the original article of Bowes, Elliott and Moss[2], fibrinoid tissue from patients suffering from rheumatic fever and rheumatoid arthritis contains less hydroxyproline than normal tissue, so that our statement was qualitatively correct. We reiterate our main theme, that since the denaturation and shrinkage of collagen is a time-dependent process[3], collagen will denature at temperatures below the instantaneous shrinkage temperature given a sufficiently long time, and that this time will be reduced (at any fixed temperature) if the percentage of hydroxyproline is also reduced. Gustavson[4] has presented experimental evidence along these lines showing that calf-skin begins to denature in water at 45° C. after one week. Stress relaxation studies[5] also show that rat-tail tendon slightly extended in 0·9 per cent saline begins to denature at about 40° C., although there is no tendency for the tendon to shrink when unloaded. We consider this to be the beginning of the structural breakdown which, however, only takes place on a large enough scale to cause instantaneous shrinkage at the higher temperature known as the shrinkage temperature.

With reference to invertebrate collagens we point out that our speculations applied only to vertebrates and were applicable only because of the similar chemical nature of these collagens. With invertebrate collagen the greater variability in chemical composition[6] means that differences in chemical properties cannot be related to one particular constituent.

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# HÆMATOLOGY

## Possible Origins of the Anti-Gm Sera

SINCE Grubb and Laurell discovered the Gm factor in 1956 (ref. 1), all those who have worked in this field have carried out the tests with sera from patients suffering from rheumatoid-arthritic diseases. Thus Harboe and Lundevall[2] and then Harboe[3] found and described the Gmx and Gmb factors in 1959. Also using a rheumatoid-arthritic serum, Steinberg[4] was able to demonstrate in the sera of Negroes the presence of a Gm-like factor, a factor which is not found in the white population. In 1959, however, Grubb found an anti-Gm factor in the serum of a young girl who was suffering from hepatitis with plasma cells[5].

Investigation of the Gm factor is based on the fact that a certain percentage of normal sera has the property of inhibiting the agglutinating power of some rheumatoid-arthritic sera. It is characteristic of this agglutinating power that the sera agglutinate O CDE red cells sensitized by an incomplete anti-D. Such agglutinating powers have been found and described by Milgrom *et al.* in the sera of clinical patients and by Unger *et al.* in the sera of healthy persons. But these authors have also noticed the non-inhibition of these agglutinating powers by the adjunction of human γ-globulins or normal sera.

From examination of more than 12,000 blood donors from the population of the Seine-Maritime, France[6,7], and also patients from different departments of our hospital, we have found this agglutinating power in some sera. But these sera could be inhibited by the adjunction of other normal sera[8]. Further investigations have shown that these sera were anti-Gm.

Hence, at the present time, we have been able to demonstrate the presence of anti-Gma in the sera of

Table 1

| | | Dilutions of the normal sera | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64 | 1:128 | 1:256 | 1:512 | 1:1,024 |
| Blood donor's sera | Gm+ serum | − | − | − | − | − | − | − | ++ | ++ | |
| | Gm− serum | ++ | ++ | +++ | +++ | +++ | ++++ | +++ | +++ | +++ | |
| Rheumatoid-arthritic sera | Gm+ | − | − | − | − | + | ++ | +++ | +++ | +++ | |
| | Gm− | − | ± | + | ++ | +++ | ++ | +++ | +++ | +++ | |

9 apparently healthy blood donors, and one patient suffering from pulmonary tuberculosis. The Gmx has been found in one blood donor and in the serum of one patient treated for allergic reactions. Each time, the specificities of these anti-Gm sera were checked by testing on a panel of 50 normal sera which have been tested with anti-Gma and anti-Gmx rheumatoid-arthritic sera and furthermore by genetic control of matings involving about 100 children.

From the serological point of view, it is important to direct attention on the difference which seems to exist between the inhibitory tests[7,8]; with the rheumatoid-arthritic sera, the inhibition appears to be a quantitative phenomenon. Suitable dilutions of sera are necessary for the test, in order to demonstrate the presence or absence of the inhibitory factor. For that reason, Harboe[10] has set up his method of scores.

On the other hand, when anti-Gm sera from patients (tuberculosis, allergic diseases) or blood donors are used, inhibition appears as a qualitative phenomenon. It occurs with sera Gm+, employed undiluted as well as diluted to 1/128 or more (see Table 1).

It would be interesting to study these different agglutinating properties as regards their physico-chemical aspects and particularly to investigate whether or not the anti-Gm property of rheumatoid-arthritic sera is different from that found in patients suffering from other diseases or in healthy persons.

At present, contrary to the general opinion, we find that anti-Gm sera can be present in the rheumatoid diseases, in chronic and evolutional diseases and in healthy persons.

*Note added in proof.* Since this communication was submitted for publication, a new serum group has been found and called InV. The agglutinating power has been found in the serum of a healthy blood donor. This InV factor is independent of the Gma, Gmb and Gmx factors. It is present in the sera of Whites as well as Negroes. Also we have found an anti-Gmb in the sera of two other healthy blood donors.

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## Thalassæmia in a Tibetan discovered during a Hæmoglobin Survey among the Sherpas

As a part of an investigation into the health of the Sherpas, undertaken during the course of the British Sola Khumba Expedition during the spring of 1959, venous blood samples were obtained from 129 inhabitants of Khumbu villages, out of an estimated population of 2,500 (von Fürer-Haimendorf, C., personal communication).

The blood samples were collected into sterile vacuum tubes ('Venules', Winthrop Laboratories, Ltd.), which were then sealed with adhesive wax ('Okeria Wax 1350/2', Astor Boisselier and Lawrence, Ltd.). The sealed tubes were stored on ice in large wide-mouthed vacuum flasks for protection from cold at high altitude and from heat during the return march to Katmandu in June. The flasks themselves, supplied by the British Vacuum Flask Co., were housed in stout wooden containers with hinged lids and packed with sawdust. These were wrapped in polythene foam sheeting which could be doused with water at frequent intervals during the hot stages of the march. By these means small pieces of ice were still preserved on arrival back at Katmandu on the eighth day after the last opportunity to recharge the flasks. The samples were flown back to London in ice-filled flasks, when they were taken at once to St. Bartholomew's Hospital.

All the samples were examined for hæmoglobin F by the 1′ alkali denaturation test[1]. In view of the presence of hæmoglobin H in Chinese and South-East Asian populations in general, and of the finding of hæmoglobin E in Malayans and occasionally in Ghurkas, all samples were tested by electrophoresis at alkaline *p*H using barbiturate buffer[2]. They were further examined by electrophoresis in *tris* buffer[3] to determine the level of hæmoglobin $A_2$. No abnormalities were discovered in 128 blood samples, but in one, 5·9 per cent alkali-resistant hæmoglobin was found, and the hæmoglobin $A_2$-level was seen to be raised above the normal 3·5 per cent (Fig. 1). The finding of a significant amount of hæmoglobin F, and of a raised hæmoglobin $A_2$-level is diagnostic of thalassæmia minor. The only other evidence of a thalassæmia gene in a Himalayan population was made in the Ghurkas[4], who, however, are racially quite distinct from the Sherpas.

The Sherpas live on the southern watershed of the main Himalayan range in north-eastern Nepal in villages lying mostly at altitudes between 10,000 and 12,000 ft. They are of pure Tibetan ancestry. The man in whom the evidence of thalassæmia was discovered was a servant in the Bhuddist monastery at Thyangboche, aged about seventy years, and he was born in Tibet. He was suffering from right-sided heart failure with generalized œdema, which was thought to be due to 'chronic mountain sickness' or so-called Monge's disease. The blood pressure was

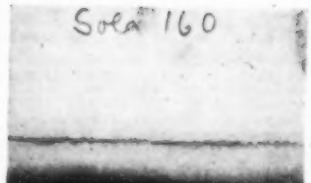


Fig. 1. Hanging paperstrip electrophoresis of haemoglobin of Tibetan with 5·6 per cent F and 4·1 per cent $A_2$. *Tris* buffer, *p*H 8·9, stained with 'light-green'

135/95, and the serum cholesterol 119 mgm. per cent.

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## HISTOLOGY

### Neurokeratin Network of Myelin Sheaths

The recent communication of Tewari and Bourne[1] on the neurokeratin network of peripheral nerve fibres is valuable not only for its intrinsic content but also because it validates the histological procedures, findings and arguments derived therefrom, by which it was concluded that neurokeratin formations are part of the architecture of the nerve fibres and not artefacts[2,3]. It is sad to think that Nageotte[4], who saw the structures in peripheral nerve fibres described by me[2,3] and by Tewari and Bourne, looked on them as artefacts. One of the strongest anatomical arguments against the notion of artefact is that the disposition of neurokeratin in spinal cord axons and in the preterminal axons found in spinal cord, in brain stem and in cerebral and cerebellar cortices is quite different from that characteristic of peripheral nerve trunks, even although the material examined was fixed and prepared for sectioning under strictly comparable conditions in all instances.

Work in progress shows that not only the disposition, but also the amount, of neurokeratin varies in different parts of the nervous system. This can be shown optically by using the falgic acid staining process described elsewhere[5]. In this process sections are stained first with acidified acid fuchsin and then with a very dilute solution of light green. Acid fuchsin can combine with one, two or three molecules of light green to form red, violet or blue compounds, respectively; these have been named the falgic acids. The red compound is formed where acid fuchsin is most abundant, the blue where it is least so. Thus the relative uptake of acid fuchsin (relative erythrophilia) of tissue elements can be determined by colour. Neurokeratin is erythrophilic and the falgic acid method shows that it is present in great density in spinal cord axons, somewhat less so in peripheral and least in the axons of the white matter of the cerebral and cerebellar cortices, and indeed in fine medullated fibres everywhere. These latter fibres are therefore difficult to display by the falgic acid technique.

Nevertheless, the essential feature of this technique can be used to make such fine fibres clearly visible as well as showing the markedly erythrophilic types of axon. The falgic acids are formed by the union of one or more molecules of light green with the amino-groups of acid fuchsin, one molecule of light green uniting with one of these amino-groups. The acid fuchsin, already attached to basic elements of the tissue by its sulphonic groups, behaves as a 'trivalent' base towards the acid light green. Other acid dyes can replace light green in this type of combination. In particular, violamine 3*B* can be used; the red, violet and blue colours produced by the falgic acid technique are then replaced by red, purple and deep violet, respectively. If sun yellow *G* be mixed with the violamine solution, the erythrophobic tissue elements are stained yellow, giving a very good contrast with the elements coloured by the 'faviolic acids', as we may call them. This shows the finest nerve fibres and is a very simple technique for the display of both dendrosomatic and axonic parts of neurones. It gives a picture equivalent in detail shown to that provided by MacConaill's acid fuchsin-lead hæmatoxylin method[3], but it is free from the risk of the formation of precipitates which that method entailed. By it the staining properties of neurokeratin can be used for a demonstration of the presence of medullated fibres, and for an assessment of the relative amounts of neurokeratin present in different fibres.

Details will be published elsewhere when the work has been completed. Meanwhile it would seem that the descriptions of the structure of myelinated fibres should be drastically revised in current textbooks, notwithstanding the apparent discrepancy between the findings of optical and electrical microscopy.

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## Structure of the Walls of the Bile 'Canaliculi' in Mammalian Liver Cells

THE structure of the walls of the bile canaliculi of the liver has long been of interest; the question of importance being whether the canaliculi had definite walls of their own, or whether they were formed from modifications of the walls of the hepatocytes themselves. Early workers[1-3] believed that the canaliculi had definite walls of their own; but Zimmermann[4] suggested that they were formed by modifications of the walls of the hepatocytes, and described dense structures at the edges of the canaliculi which he called "terminal bars". Morton[5] was able to show that the lining of the bile canaliculi was in the form of a 'brush border', and apart from Zimmermann's terminal bars he found a collection of basophilic material in the cell cytoplasm lying close to the bile ducts. Rouiller[6], in an electron microscope study of the rat liver bile canaliculi, showed that the cell membranes were closely opposed in the neighbourhood of the canaliculus, but with only osmium as an electron stain, he found no modification or thickenings of the cell wall in the proximity of the duct. In a study of normal and regenerating rat liver using 'Araldite' embedding followed by phosphotungstic acid staining, it was found that some parts of the cell walls related to the bile ducts took up this stain particularly well.

In liver cells stained with phosphotungstic acid, dense bands of materials are seen at various points on the plasma membrane. These bands are always exactly opposite a similar band of identical length on the membrane of an adjoining cell (Figs. 1 and 2). They cause a thickening of the plasma membrane from its usual 80–90 Å. to 500–600 Å., and are always present close to the points where the plasma membranes of two cells divide to form a bile canaliculus, although they are also to be found at other points on the cell membrane.

These structures, revealed by phosphotungstic acid staining in close relationship to the bile canaliculi of liver cells, seem in agreement with the previous work using the light microscope. Thus the dense phosphotungstic acid-positive bands on the cell membranes close to the bile canaliculi are in the same position as the "terminal bars" of Zimmermann, and are probably identical with these structures. Zimmermann's original term "Kittleisten" suggested a cementing substance, and it is therefore perhaps not surprising to find areas of phosphotungstic acid-positive material, scattered all along the cell membrane.

Similar material has been found on the plasma membranes of mouse pituitary cells by Barnes[7]. In this case the material is neatly laminated instead of being a single band on each membrane; but the same conclusion is reached, namely, that the function

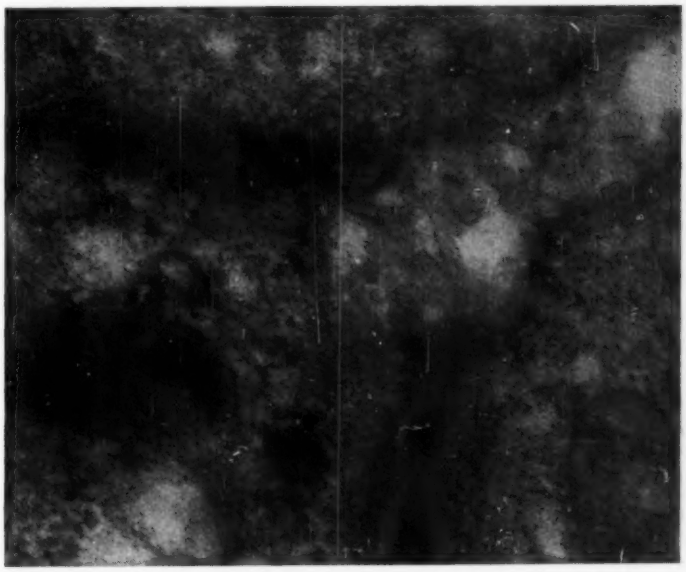

Fig. 1. Part of an elongated bile canaliculus formed at the junction of the three liver cells. The cell membranes close to the canaliculus are much thicker than normal, being as much as 500 Å. thick, and stain very densely with phosphotungstic acid. (× c. 40,000)

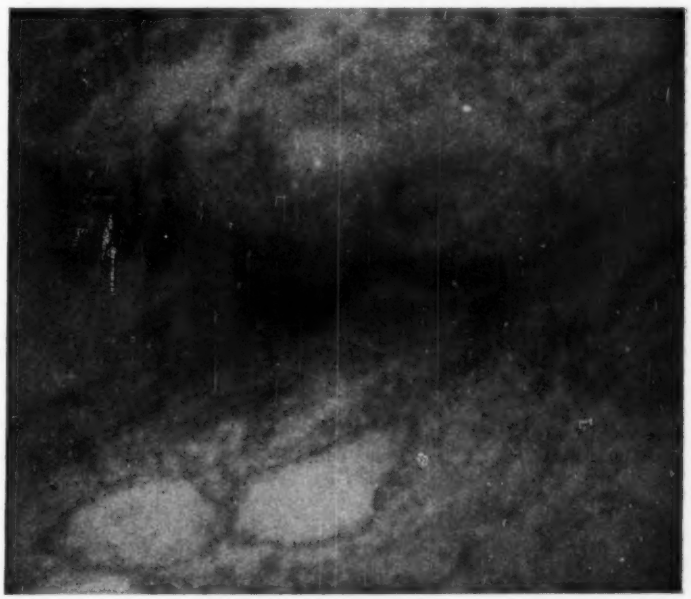

Fig. 2. A high-resolution picture of the cell membranes of two liver cells close to a bile canaliculus. The dense phosphotungstic acid-positive material is clearly visible. (× c. 128,500)

of this material may be to assist in the binding of cells together. The material for this work was obtained from normal adult Wistar rats. It was fixed by the method described by Barnes and Davis[8] and embedded in 'Araldite' as described by me[9].

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## PATHOLOGY

### Porphyrin Fluorescence of Experimentally produced Squamous Cell Carcinoma

Ulcerated squamous cell carcinomas of the human skin frequently show a red fluorescence when examined under ultra-violet radiation[1–3]. This red fluorescence is usually restricted to small areas of the necrotic surface. Hitherto the substance or substances responsible for this phenomena have not been identified. This is probably due to the fact that very small amounts of material are available for study in any single case. Recently, Ghadially[4] observed that experimentally produced squamous cell carcinomas of the skin of many animals show a similar red fluorescence. It seemed to us that by pooling material from a number of tumours, sufficient might be obtained for a chemical analysis. Six rabbits with large ulcerated carcinomas produced by repeated painting of the skin with a 2 per cent solution w/w of 9 : 10 dimethyl 1 : 2 benzanthracene in a mixture of equal parts of lanolin and paraffin were available for study. After many attempts, we were ultimately able to collect one large (5 gm.) pooled sample for analysis. Another large sample was obtained from a single rabbit which died as a result of a very large fungating carcinoma of the ear. Here about 5 gm. of red fluorescent debris had collected on the carcinoma and within the ear over a prolonged period of time. The results obtained in each case were essentially similar.

Red fluorescence has been attributed to the presence of porphyrins in a chloroma[5], a fungating adenocarcinoma of the breast[3] and a hepatic adenoma[6] of man. Therefore it seemed reasonable to suppose that similar material might be associated with the red fluorescent squamous carcinomas.

An ethyl acetate (75 ml.) – acetic acid (25 ml.) extract of red fluorescent debris (5 gm.) from the rabbit carcinoma was examined for protoporphyrin, coproporphyrin, and uroporphyrin by the methods of Schwartz and Wikoff[7] and Dresel and Falk[8]. The absorption spectrum of a fraction corresponding to protoporphyrin was measured in ethyl acetate solution with a Unicam spectrophotometer *SP* 500 in the range 350–800 mμ (in 5-mμ steps) in 1-cm. cells versus an ethyl acetate blank. Table 1 gives wave-lengths and optical density values of the maxima and minima exhibited by this porphyrin solution, and, for comparison, the corresponding values are quoted for the spectrum of an authentic sample of protoporphyrin (Light and Co.) in ethyl acetate. These spectra were closely similar, and it may be concluded that protoporphyrin occurs in the carcinoma debris.

Table 1

| Material from carcinoma debris | | | Authentic protoporphyrin | | |
|---|---|---|---|---|---|
| 400 mμ | max. | 1·750 | 400 mμ | max. | 2·520 |
| 460 | min. | 0·025 | 465 | min. | 0·030 |
| 505 | max. | 0·135 | 505 | max. | 0·197 |
| 525 | min. | 0·048 | 525 | min. | 0·058 |
| 540 | max. | 0·077 | 540 | max. | 0·123 |
| 565 | min. | 0·019 | 560 | min. | 0·019 |
| 585 | max. | 0·052 | 580 | max. | 0·073 |
| 615 | min. | 0·008 | 615 | min. | 0·007 |
| 635 | max. | 0·027 | 635 | max. | 0·049 |

The fraction which should contain coproporphyrin fluoresced red in ultra-violet light, but the porphyrin content was so low that only a very feeble Soret band was detected at 400 mμ in the most concentrated extract we could obtain.

Finally, the fraction which should contain uroporphyrin according to Dresel and Falk failed to fluoresce in ultra-violet light.

Thus the material responsible for the fluorescence of rabbit ear carcinoma seems to consist mainly of protoporphyrin with perhaps a trace of coproporphyrin.

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### Phenylketonuria in Infant Monkeys

We had previously established[1] that the characteristic aberrations found in human phenylketonuria, namely, high plasma phenylalanine, phenylketones in the urine, and characteristic odour were observed in adolescent monkeys fed excessive amounts of L-phenylalanine in their diet. From the results of behavioural tests utilizing discrimination and maze performance, as well as poor adaptability to the test situation, these monkeys appeared to be retarded in their learning ability. It seemed important to determine whether phenylketonuria could be produced in infant monkeys when the brain is apparently more sensitive to chemical insult. Long-term observation could then be made throughout the period of development and it might be possible to correlate the biochemical changes with behavioural patterns.

Four infant macaques born in this laboratory were separated from their mothers at birth and were given a high phenylalanine milk diet from the second day of life. Whole cow's milk or powdered milk formula containing 0·25 gm. L-phenylalanine per 100 ml. in final dilution was fed for the first two weeks. Later,

increasing quantities of the amino-acid were included to a maximum of 0·5 gm. of L-phenylalanine per 100 ml. The average infant monkey consumed enough milk to make the daily intake approximately 2·75 gm. of phenylalanine per kgm. body-weight. The infant monkeys were bottle-fed by hand every 2 hr. for the first 2 weeks, then fed by means of an infant feeding bottle placed in a mother surrogate so that the infant could crawl on to this false mother for the nipple feedings in the usual position. Plasma phenylalanine was determined[2,3] at weekly intervals for the first six months, then at bi-weekly intervals up to the first year. The urine was tested daily during the first year and revealed strongly positive phenylketones as determined by the 'Phenistix' (Ames Co., Elkhart, Indiana) or ferric chloride methods, and it had the peculiar musty odour typical of that of children with this disease. Quantitative blood and urine analyses are shown in Table 1. The fasting plasma phenylalanine of normal infant monkeys ranged from 1·0 to 1·5 mgm. per cent, while the monkeys which received L-phenylalanine ranged from 8·8 to 47·5 mgm. per cent. These high plasma phenylalanine-levels are comparable to that of phenylketonuric patients. The urine collected from male monkeys indicated that normal animals excreted negligible amounts of phenylpyruvic acid as determined by the method of Berry and Woolf[4], while the monkeys which received L-phenylalanine excreted 79–465 mgm. phenylpyruvic acid in 24 hr.

Table 1

| Monkey | Mgm. phenylalanine/100 ml. plasma | Mgm. phenylpyruvic acid/24 hr. urine |
|---|---|---|
| *A* 8 ♂ | 16·6–39·0 | 113–257 |
| *A* 18 ♂ | 8·8–32·9 | 79–465 |
| *A* 22 ♀ | 10·9–46·1 | — |
| *A* 24 ♀ | 10·4–47·5 | — |
| Controls | 1·0–1·5 | 0 |

The monkeys receiving the high phenylalanine milk grew nearly as well as monkeys fed a normal laboratory diet. Those animals which consumed very high amounts of phenylalanine because they were better milk drinkers usually showed less gain in weight than the monkeys the milk intake of which was not as great. This may be a clue that the phenylalanine was near toxic levels at 2·75 gm. of amino-acid per kgm. body-weight per day. The fur coat of the animals was in all respects normal in colour and in quantity, and no abnormal skin lesions or delay in dentition were noted. Neurological examination revealed no sensory or motor abnormalities in these animals up to one year of age. Two of the four animals had typical grand mal convulsions at widely spaced intervals, and the monkeys usually slept for a short period following the seizure, but promptly recovered with no residual effects.

The psychological testing of each animal was begun shortly after the first week of life and consisted of: (1) delayed response tests; (2) discrimination learning set tests; (3) object discrimination tests; (4) Hebb-Williamson maze test, according to methods performed in this laboratory by Harlow[5] and his associates. The total performance of the phenylketonuric animals was much below that of normal animals of the same age in all tests. It was quite clear that the retarded animals could not learn delayed response and discrimination learning set tests. These monkeys demonstrated motivational defects, inappropriate behaviour, subnormal learning, and sub-optimal intellectual performance.

An unusual opportunity for obtaining additional information on certain aspects of brain metabolism in mental retardation is thus provided by the production of phenylketonuria in a sub-human species. Work is now in progress to obtain information from monkey experiments so that treatment of phenylketonuria in human infants might be more satisfactory. The role of liver hydroxylase and brain decarboxylases on amino-acid metabolism can be thoroughly investigated in these animals. Further experiments designed to produce other types of retardation in monkeys are now under way.

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## RADIOBIOLOGY

### Early Incorporation of Sulphur-35 Sodium Sulphate into Plasma Proteins of Man

IN investigating the fate of radiosulphate in multiple myeloma[1], the incorporation of sulphur-35 in human plasma protein fractions was investigated.

Carrier-free sulphur-35 as sodium sulphate in doses ranging from 0·867 to 2·07 mc. was administered intravenously to 10 patients with multiple myeloma and 14 patients with other neoplastic diseases. A patient with chondrosarcoma received labelled sulphate in three intravenous doses at weekly intervals of 505 mc., 391 mc., and 322 mc., respectively. (We wish to express our gratitude to Dr. C. Botstein, head of the Radiotherapy Dept., Montefiore Hospital, for making this patient available for study. The sulphur-35 for this patient was supplied by Abbott Laboratories.)

Sulphur-35 assays were made with a calibrated gas-flow counter and corrected for back-scatter and self-absorption. Blood samples were obtained at intervals during the initial 24 hr. and daily thereafter for the next 6 days.

Analysis of plasma proteins was performed with electrophoretic and staining techniques previously described[2]. Simultaneously run filter paper strips were scanned for radioactivity in a suitably adapted gas-flow counter and exposed for 90 days to Kodak No-screen double-coated X-ray film for radioautography. Continuous curtain electrophoresis was performed on 1- to 3-ml. samples of plasma with standard techniques[3].

In none of the plasma samples obtained from the myeloma patients and subjects with other neoplastic diseases was radioactivity demonstrable by scanning of the electrophoretic strips, radioautography, or continuous electrophoresis.

For the subject with chondrosarcoma, given more than 1 c. of sulphur-35 in 3 doses, however, progressive incorporation of sulphur-35 into the plasma protein fractions was readily detected after each dose by the assay of the electrophoretically separated proteins on the filter paper strips (Fig. 1). The relative distribution of sulphur-35 for the various protein moieties as a function of time is presented in detail for the initial therapeutic dose of 505 mc. (Fig. 2). Similar patterns were observed after each therapeutic dose. The albumin fraction promptly incorporated sulphur-35 with the maximum value reached in 4 hr. and thereafter showed a more gradual decline during 48 hr. Little further change was observed during the next 4 days. A slower incorporation of sulphur-35 with the maximum peak occurring in 18 hr. was noted for fibrinogen. The degradation was also slower than that of albumin, taking 4 days to reach minimum values. The α- + β-globulin fraction paralleled the fibrinogen curve at a lower level of radioactivity. Its peak-level was also reached in 18 hr. Little incorporation of sulphur-35 into γ-globulin was observed. However, it should be noted that this patient had a low concentration of γ-globulin. The highest level for this fraction was attained in 8 hr. and fell to base-line levels in 24 hr.

Sulphur-35 administered as sodium sulphate has been shown to be incorporated into the plasma proteins of animals[4], but such incorporation has not been demonstrated in man. Reasons for this failure include: (1) Most of the sulphur-35 administered is excreted in the urine within 48 hr.[1,5]. (2) The fraction of the dose remaining within the body is widely distributed in the sulphomucopolysaccharides of cartilage, aorta, sclera, cornea and intestinal mucosa[6]. (3) The maximum permissible dose of 2 mc. for this work was insufficient for the detection of radio-

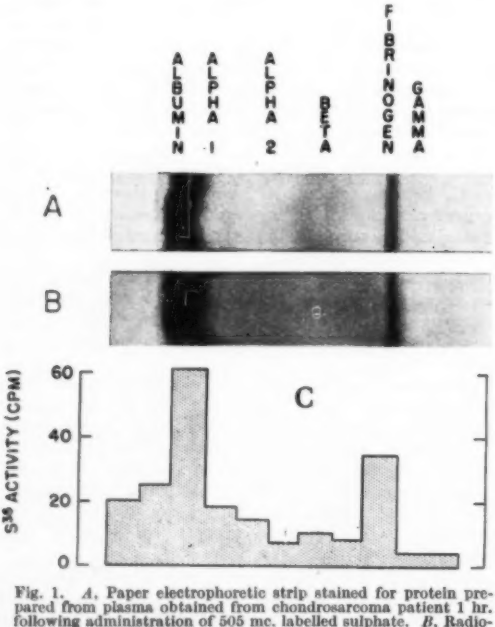


Fig. 1. *A*, Paper electrophoretic strip stained for protein prepared from plasma obtained from chondrosarcoma patient 1 hr. following administration of 505 mc. labelled sulphate. *B*, Radioautograph of strip (94-day exposure); density corresponds to sulphur-35 activity. *C*, Relative distribution of activity along a strip determined by scanning with collimated gas-flow counter; adequate counts collected to assure 5–10 per cent accuracy

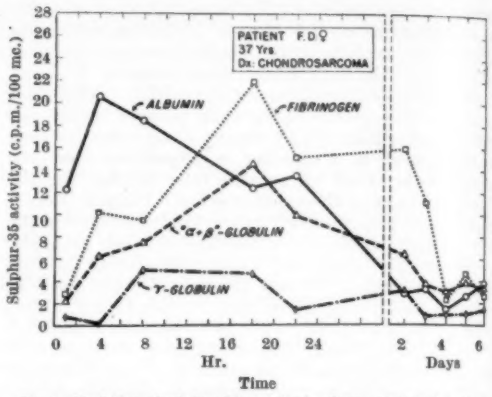


Fig. 2. Variation of sulphur-35 activity in plasma protein fractions with time as derived from scans of corresponding electrophoretic strips

activity in human plasma protein fractions, although even smaller amounts were found adequate for the rat[4].

In the patient with chondrosarcoma, sulphur-35 was readily detected in all the plasma protein fractions after each therapeutic dose. The problem then arises as to how the sulphur-35 is bound to protein. One possibility is that the sulphur-35 is incorporated only into the protein-bound sulphated mucopolysaccharides. If this were so, the radioactivity would be distributed in the plasma protein fractions in proportion to the distribution of protein-bound polysaccharides. Indeed, this was found to be the case in the rat, where about 40 per cent of administered sulphur-35 sulphate activity was bound to a serum constituent having the electrophoretic mobility of α-1-globulin, suggesting that the binding occurs in a protein-bound sulphomucopolysaccharide[7]. However, the distribution of sulphur-35 in the plasma protein of the patient herein reported was not that of mucopolysaccharides. The greatest concentration of sulphur-35 was found in albumin and fibrinogen, indicating that the sulphur-35 was incorporated into the sulphur-containing amino-acids of the protein rather than the protein-bound mucopolysaccharides. This, of course, does not rule out some tagging of the sulphated mucopolysaccharides.

After oral administration of sulphur-35 labelled cysteine to man, the incorporation of the label into serum protein fractions has been shown to occur with great rapidity[8]. A striking similarity between our results using sulphur-35 labelled sulphate and those using the labelled amino-acid is noted. Thus, the albumin peak for sulphur-35 cysteine also occurred in 4 hr. and the α- + β-globulin peak at a time similar to ours. Of interest is the fact that the maximum for γ-globulin after labelled cysteine was low in a nutritionally normal patient, so the low values we observed may not be related necessarily to the hypogammaglobulinæmia of our patient with chondrosarcoma. Furthermore, the ratios of the respective maxima to each other are almost identical for both studies. It would appear then that inorganic sulphate is rapidly bound to the various plasma protein fractions, presumably after first being incorporated into an amino-acid precursor. Also, the fact that our findings with sulphate parallel those done by others with labelled cysteine supports the view that sulphate is incorporated into the protein fractions, rather than

non-specifically bound. This is confirmed by our unpublished work in which we failed to demonstrate labelling of the plasma protein fractions after incubation with sulphur-35 labelled sulphate.

Plasma proteins contain functional SS groups and SH groups which are probably part of the cystine and cysteine molecules. Although there is little evidence to suggest that animal tissues can synthesize sulphur-containing amino-acids, there is good evidence that it does occur in animals and that this requires the presence of micro-organisms in the alimentary tract[9]. The steps whereby the sulphur-35 of labelled sodium sulphate becomes incorporated into the sulphur-containing amino-acids of human plasma proteins are yet to be elucidated. This investigation demonstrates that it does occur. It is possible that in the human, as in lower animals, the activity of intestinal micro-organisms plays an important part. However, in the present work, one must postulate initial secretion of labelled sulphate into the bowel, directly or via bile, because all doses were given intravenously. The rapidity with which the incorporation of the inorganic sulphate into plasma protein occurs suggests that an alternative metabolic pathway may exist.

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## BIOLOGY

### Sun Navigation by Birds

C. J. PENNYCUICK[1], discussing the physical possibility of an estimate of the change in azimuth of a celestial object by a bird, says: "Birds very often fly round in circles whilst orienting, and therefore cannot have their eyes stabilized in azimuth. The change in azimuth can therefore be measured only by reference to a fixed object [*sic*], when the bird is stationary on the ground. Over the sea it is not physically possible to measure it at all without some kind of compass. However, birds do navigate over the sea. Hence Matthews' hypothesis as it stands is untenable". Again in his summary: "Matthews' hypothesis . . . is rejected on the grounds of physical impossibility of making one of the measurements,. . . ".

Assertions about the physical impossibility of animal activities have so often proved false that they should be closely scrutinized, and Pennycuick's argument appears to be fallacious. What the bird needs is not a fixed object (in parenthesis it may be pointed out that a compass needle is not a fixed object) but an indication of a direction—any direction —in the horizontal plane lasting long enough (not more than a few minutes on Matthews's[2] hypothesis) to allow the change of azimuth of the celestial object to be measured. My experience of flying at a moderate height over the open sea is strictly limited; but I have never known an occasion when the sea could not be seen at all and when the necessary stable indication of direction could not have been obtained from the pattern of waves on its surface; in the belief that occasions when this indication is not available are exceedingly rare, I am confirmed by an experienced pilot of aircraft. It is therefore fair to assume that a flying bird could always obtain the necessary information in flight over the sea and that Matthews's hypothesis has not, on this ground, been invalidated.

Pennycuick's own hypothesis, requiring only an appreciation of the Sun's elevation and of its rate of change, is attractive and economical, but it is surely unlikely that a bird should neglect information about the sign and magnitude of the Sun's rate of change of azimuth when this information, always available, could be used to increase the accuracy of estimate of its own position and to eliminate the ambiguity which can arise, according to Pennycuick, in certain circumstances.

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IT must be conceded that the rate of change of the Sun's azimuth could, in principle, be measured by reference to the orientation of the waves on the sea, but the possibility of using this method for navigation requires closer scrutiny. If it be assumed that the bird can use the maximum accuracy available, the problem falls into three parts:

(1) Within what limits can the direction of the waves be defined?

(2) Within what limits may its rate of change be deemed to be zero?

(3) To what distance on the ground does the minimum detectable change of rate of change of azimuth correspond?

It is to be hoped that someone better qualified than I will be able to produce definite information on the first two questions, but meanwhile some reasonable surmises may be made.

(1) The meaning of the "direction of orientation" of the pattern of waves on the sea would appear to be statistical in nature, the accuracy with which it could be defined increasing with the number of waves visible. The direction of the waves on a large stretch of sea seen from the air could clearly be defined within 10°, and probably usually within 1°. Whether it could be defined within 0·1° (1/5 of the diameter of the Sun's disk) is not so clear. In the following argument $\pm$ 0·01° accuracy will be assumed, which is perhaps optimistic.

Large errors would occur in shallow waters owing to refraction of the waves in water of varying depth, so the use of the method would probably be confined to the open ocean.

(2) The limits within which the rate of rotation of the wave-pattern may be deemed to be zero (even when it really is zero) will depend on the above accuracy with which the direction of the wave-pattern can be determined, and also on the length of time available for observation. It would be logical to choose for the latter that time during which rate of change of azimuth changes by, say, 5 per cent, but to avoid complication, an observation time of 1 min. will be assumed arbitrarily. This has the effect of making changes of navigational accuracy from place to place appear greater than they really are, since in those regions where rate of change of azimuth changes rapidly with distance (good navigational accuracy) it also changes rapidly with time (short time available for observation). Also the best accuracy on the present assumptions is obtained when the Sun is high in the sky, which makes azimuth and changes thereof more difficult to observe. For the sake of argument let it be assumed that the rate of change of the Sun's azimuth can be measured by reference to the waves on the sea within $\pm$ 0·01°/min. of time.

Apart from the problem of measurement, it is likely that an accuracy of this order would only be obtainable in regions of rather constant weather, such as the trade wind zones: such stability could probably not be relied upon in the North Atlantic, for example.

(3) If $Z$ is the Sun's azimuth, $L$ the observer's latitude, and $H$ the local hour angle, it may be shown that, in the special case of equinox:

$$\frac{\partial Z}{\partial H} = \frac{1}{\mathrm{cosec}L \sin^2 H + \sin L \cos^2 H} \qquad (1)$$

Fig. 1 is a diagram of lines of equal rate of change of azimuth, plotted for equinox. They form a family of closed curves meeting at the Sun's position. The points at which they cut the centre and edge of the diagram are calculated, but the shape in between is approximate.

The error of position for a given error of $\partial Z/\partial H$ is proportional to the spacing of these lines, that is, the rate of change of position with respect to $\partial Z/\partial H$. At noon ($H = 0$) we have:

$$\frac{\partial Z}{\partial H} = \mathrm{cosec}L$$

whence, differentiating up the Sun's meridian,

$$\frac{\partial}{\partial L}\left(\frac{\partial Z}{\partial H}\right) = -\,\mathrm{cosec}L\ \cot L \qquad (2)$$

If the permissible error of $\partial Z/\partial H$ is $\pm$ 0·01°/min. of time, or $\pm$ 0·04°/deg. of hour angle, and the required accuracy of position finding is arbitrarily taken as $\pm$ 0·005 radian (17 nautical miles), then:

$$\mathrm{cosec}L\ \cot L = \frac{0{\cdot}04}{0{\cdot}005} = 8$$

$$L = 20°$$

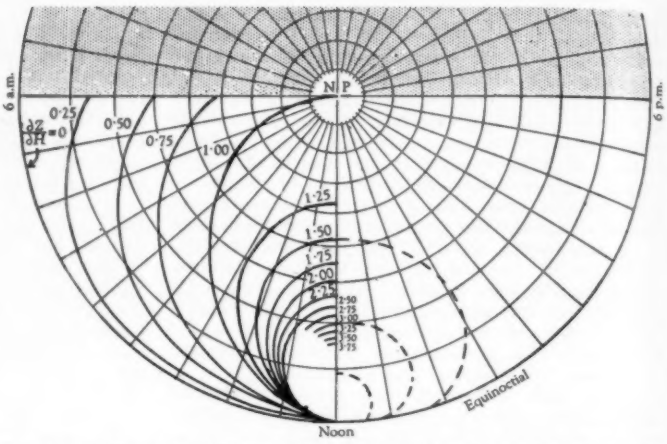


Fig. 1. Stereographic projection of the northern hemisphere, showing lines of equal rate of change of azimuth. The curves are approximate except that their intercepts on the noon and six o'clock lines are calculated. Dotted lines enclose zones in which particular accuracies of position finding could be obtained (see text)

The middle dotted line in Fig. 1 encloses the zone within which the required accuracy can be obtained. It crosses the meridian at $L = 20°$, but the rest of it is drawn approximately. There is another mirror image zone south of the equator.

If the assumptions as to accuracy have been five times too optimistic, the zone comes up to 9° lat. (inner dotted line): if they have been five times too pessimistic, it comes up to 42° (outer dotted line). There is always a minute zone near the Sun within which any accuracy, however bad, will suffice.

It is hoped that the dubious assumptions in the above argument have been made explicit and will elicit informed comment. It seems likely that the method suggested by Prof. Pumphrey, while restricted in application, might very well provide navigational information to pelagic birds living in the trade wind zones. However, it would work best in roughly the same region where maximum accuracy can be obtained from rate of change of altitude, so it will not fill in any deficiencies in the system previously suggested.

It may be worth noting that observing the direction and speed at which the Sun moves across the sky, is equivalent to measuring the rates of change of altitude and azimuth, and no reduction in the accuracy requirements can be made by describing the process in one form rather than the other.

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## Reactions of Soil Nematodes to Coal-Tar Dyes

Tests with dilute aqueous solutions of coal-tar dyes on soil nematodes reveal that reactions to 19 basic dyes of varied chemistry are of three classes.

Class I (absorption reaction), observed in many genera of the Enoplida, typically involves entry of the dye first at the anterior and then almost simultaneously at the posterior end of the nematode, with staining progressing toward the centre. Minimum

solution thresholds of this reaction range from 100 to 10 p.p.m. in 24 hr. Death occurs commonly; and in the stronger solutions is accompanied by intense accumulation of dye throughout the nematode corpus, obscuring internal structures. The reactions of all groups of soil nematodes to iodine fall into Class I. Minimum thresholds for iodine of both staining and toxicity in *Tylenchorhynchus martini* Fielding 1956 were between 10 and 1 p.p.m. in 24 hr.

Class II (basophilic reaction) has been observed in the genera *Tylenchorhynchus* (6 species), *Aphelenchoides* (2 species) and *Rhabditis* (2 species). This reaction manifests extreme sensitivity with minimum concentration thresholds ranging from 10 to 0·1 p.p.m. It is non-toxic, generally unaffected by solution *p*H and appears to be an adsorption phenomenon with staining intensities independent of dye concentrations. Each dye imparts a uniform tint of characteristic colour and intensity to the corpus, with the internal structures clearly visible. Staining occurs in 3–5 min. at dye concentrations between 10 and 1 p.p.m. and very rapidly at 100 p.p.m. The dyes appear to enter at all points on the nematode surface and the reaction is reversible in living nematodes. Stained specimens of *T. martini* placed in soil around rice plants for 7 days were re-isolated and examined. The dyes had disappeared from the corpus but were strongly retained by intestinal granules.

Class III (resistant reaction), in which there is little or no staining, has been observed in 9 known and 3 suspected phytophagous genera of the Tylenchida, in certain genera of the Rhabditida and in a *Plectus* sp. of the Chromadorida. Staining, when it occurs, is slight even at dye concentrations of 1,000 p.p.m. in 24 hr. and is largely confined to certain parts of the corpus, intestinal granules, sclerotized structures and inclusions of the body cavity.

The integrity of each class of reactions to basic dyes is maintained essentially in heat-killed and formalin-preserved nematodes, although breaking of resistance (Class III reaction) has been observed in some instances. Tests with 13 acid dyes on mixed populations of nematodes extracted from soils revealed, in comparisons with basic dyes, a more restricted spectrum of activity. Typical results, after 24 hr. in dye solutions of 200 p.p.m., show that approximately 10-fold more nematodes are stained by basic than by acid dyes.

Details of this work will be submitted for publication elsewhere.

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## Toxicity of Aluminium to Black Pepper (*Piper nigrum* L.) in Sarawak

SYMPTOMS of an unknown disorder have been increasingly observed on pepper vines since 1956; no pathogen seemed to be involved. Affected vines show an overall bright green to yellow colour and their leaves a pronounced droop. Individual leaves first show symptoms of a speckled necrosis mostly along the main veins, each brown spot having a surrounding yellow halo. Afterwards the necrotic areas spread and become more serious so that finally the leaves fall. These vines have a greatly reduced root system,

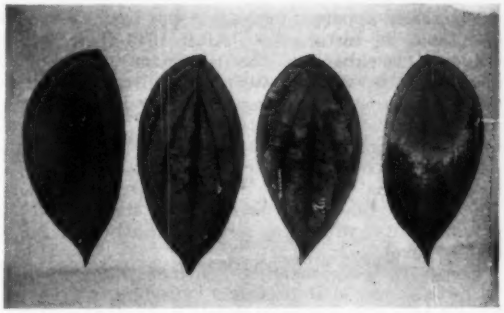

Fig. 1. The under-surface of detached pepper leaves showing a healthy leaf on the left and symptoms of increasing severity towards the right

which dies off centripetally. Different stages of the leaf symptoms are shown in Fig. 1.

Pepper vines are grown on low mounds in latosolic soils, which are poor in bases, particularly magnesium. The soil from mounds of affected vines was found always to be low in *p*H, generally below *p*H 4·5, and some mounds were as low as *p*H 3·5. Vines grown in soils of above *p*H 5·5 were unaffected. Analysis of soil from mounds of healthy and affected vines are given in Table 1.

Table 1. BASE AND ALUMINIUM CONTENT IN P.P.M. AND *p*H-LEVELS OF SOILS WITH AFFECTED AND UNAFFECTED VINES

| | *p*H | Calcium | Magnesium | Aluminium |
|---|---|---|---|---|
| Unaffected vines (mean of 12) | 5·6 (0·59) | 2,529 (61·2) | 84 (5·88) | 91 (22·72) |
| Affected vines (mean of 25) | 3·9 (0·39) | 195 (91·7) | 29 (3·91) | 330 (15·21) |

All differences are significant at $P = 0.001$. *S.E.* given in brackets

The cause of this disorder is apparently a toxicity of aluminium ions at low *p*H. These ions prevent the uptake of calcium and magnesium, leading to the deficiency symptoms of these elements, the yellowing and necrosis which appear in the pepper leaves. This free aluminium also causes the root systems to die, so that the foliage wilts, producing the characteristic droop. With the reduced uptake of calcium and magnesium, and a presumed reduction in the cation exchange capacity of the affected root system, the amount of potassium taken up actually increases, so that the ratio of K/(Ca + Mg) can be used as a diagnostic index. The critical value appeared to be approximately 1·00. These effects are illustrated in the leaf analyses presented in Table 2.

Table 2. BASE CONTENT IN PERCENTAGE DRY MATTER, AND RATIO OF MONO- TO DI-VALENT CATIONS IN PEPPER LEAVES

| Condition of vines | Calcium | Magnesium | Potassium | (K/Ca + Mg) |
|---|---|---|---|---|
| Unaffected (mean of 23) | 1 1·363 (0·053) | 4 0·231 (0·010) | 7 1·450 (0·240) | 10 0·930 (0·071) |
| Affected (mean of 18) | 2 1·046 (0·060) | 5 0·179 (0·013) | 8 1·568 (0·270) | 11 1·290 (0·081) |
| Seriously affected (mean of 12) | 3 0·523 (0·082) | 6 0·142 (0·014) | 9 1·829 (0·310) | 12 3·390 (0·029) |

*S.E.* are given in brackets.
Differences significant at $P = 0.001$: 1 and 2, 1 and 3, 4 and 6, and 10 and 12.
Differences significant at $P = 0.01$: 4 and 5, 7 and 9, 10 and 11.

The recent apparent increase in this toxicity can be accounted for historically. After 1945 there was a tendency to abandon the traditional method of manuring pepper. This was to apply large quantities of burnt earth, supplying adequate bases to the mound. Gradually, relatively small quantities of processed organic manures and cheaper inorganic fertilizers have replaced the burnt earth. Presumably, therefore, the continual loss of bases and their inadequate replacement have led to a steady increase in soil acidity, which has now apparently reached a critical level.

Steps are being taken to continue this work and to provide remedial measures. Preliminary results indicate that the incorporation of magnesium limestone into the mound will prevent this toxicity.

The permission of the Director of Agriculture to publish these results is gratefully acknowledged.

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## Digestion of the Alga, *Macrocystis pyrifera*, by the Sea Urchin, *Strongylocentrotus purpuratus*

It has been known for some time[1] that sea urchins when fed and then starved seem to retain for long periods the food present in the intestine. Furthermore, *in vitro* experiments have shown that a battery of digestive enzymes exist, some of which can digest complex polysaccharides such as iridophycin[1] and algin[2]. During a series of experiments on the digestion of various substrates by sea urchins we had occasion to feed and afterwards starve an adult urchin and then recover all the material remaining after digestion. So far as we are aware no evidence exists on the percentage of algal food that can be completely degraded to assimilable products by a sea urchin. An urchin was prestarved until no faecal pellets were passed. The animal, a female, weighing 99·3 gm., test height and test diameter measuring 26·5 mm. and 63·1 mm. respectively, was then fed a 33·3 mgm. (dry weight) piece of *Macrocystis pyrifera*, a food for which the sea urchin exhibits a high degree of preference[3], and fed no further food for 18 days. The algal piece was consumed within 8 hr. No faecal pellets were passed during the observation time, and the animal was killed at the end of this time.

We removed the complete intestine of the urchin and recovered all the undigested materials. By comparison of the dry weight of the undigested residue with the dry weight of the food eaten, it is possible to determine the percentage of the alga that was digested, and, presumably, assimilated. 8·5 mgm. of undigested material was recovered, hence more than 76 per cent dry material of the alga was removed by the digestive processes of the urchin.

This completeness of digestion by a sea urchin supports the cited study on alginase since *Macrocystis* is known to contain at least 14·5–36 per cent dry weight of algin[4]. The extensive digestion of a meal when another is not forthcoming, coupled with the urchin's ability to resorb its gonads during starvation (Boolootian and Giese, unpublished work), may account for the urchin's ability to adapt itself to environments where food might become restricted.

This work forms part of a programme of investigation supported by funds from the National Science Foundation Grant 9561 to one of us (R. A. B.).

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## Biosynthesis of Arbutin from Some Phenylpropanoid Compounds in *Pyrus communis*

Higher plants are capable of synthesizing aromatic compounds from shikimic acid, possibly through a pathway similar to that described by Davis *et al.*[1]. Certain benzene rings, however, are formed from acetate in accordance with the hypothesis of Birch and Donovan[2]. Thus the *B* ring of quercitin is synthesized from shikimic acid[3] whereas the *A* ring is an acetate-formed ring[4].

Arbutin or hydroquinone-β-D-glucoside occurs in many plants, such as members of the Ericaceae, and accumulates to the extent of 0·05–0·17 per cent of the fresh weight of pear (*Pyrus communis* L.) leaves[5]. So far as we know there has been no report on the origin of the ring of hydroquinone. Gloor and Wiss[6] have shown that mevalonic acid labelled with carbon-14 is incorporated by the rat into ubiquinone (a 2,3-dimethoxy-5-methyl benzoquinone with an isoprene side-chain of 50 carbon atoms). They have suggested that, whereas the isoprene side-chain is built up from mevalonic acid, the ring component is not synthesized by animals.

We have found that arbutin is synthesized in young leaves of pear from shikimic acid and more readily from phenylpropanoid compounds, whereas activity from acetate-$^{14}C$, pyruvate-$^{14}C$, and succinate-1,4-$^{14}C$ is not incorporated into arbutin under the same conditions of administration.

The methods used were as follows: ten leaf disks (diameter 1·2 cm.) were vacuum infiltrated with tap water, blotted and floated in a Petri dish in 1·2 ml. of a solution containing 1–2 μc. of a radioactive compound. The covered Petri dish was placed under fluorescent lights for approximately 17 hr., after which the leaf disks were rinsed in tap water and extracted with boiling 80 per cent ethanol. The ethanol extract was concentrated, and chromatographed two-directionally in 80 : 20 phenol/water followed by 4 : 1 : 5 butanol / acetic acid / water. Radioactive spots were located by radioautography, and activity measurements were made by direct counting on the chromatograms. Arbutin, which is detected by its colour reactions with diazotized *p*-nitroaniline or diazotized sulphanilic acid, is well separated on chromatograms from chlorogenic acid and the other phenolics present in extracts.

Results of some of the feedings to pear tissue are given in Table 1.

Arbutin-$^{14}C$ obtained from a phenylalanine-U-$^{14}C$ feeding was hydrolysed with 2 *N* hydrochloric acid,

Table 1. INCORPORATION OF COMPOUNDS LABELLED WITH CARBON-14 INTO ARBUTIN IN LEAF DISKS OF *Pyrus communis*

| Compound administered | Age of tissue (leaf disks) | Percentage of ethanol soluble activity in arbutin |
|---|---|---|
| Pyruvate-1-$^{14}$C | young | 0 |
| Pyruvate-2-$^{14}$C | young | 0 |
| Pyruvate-3-$^{14}$C | young | 0 |
| Succinate-1,4-$^{14}$C | young | 0 |
| Acetate-1-$^{14}$C | young | 0 |
| Acetate-2-$^{14}$C | young | 0 |
| Glucose-U-$^{14}$C | young | 0·8 |
| Shikimic acid-U-$^{14}$C | young | 5 |
| Phenylalanine-U-$^{14}$C | young | 12 |
| Phenylalanine-U-$^{14}$C | young | 21 |
| Phenylalanine-U-$^{14}$C | mature | 0 |
| Phenylalanine-U-$^{14}$C | dormant leaf buds | 12 |
| Phenylalanine-3-$^{14}$C | young | 0 |
| Tyrosine-U-$^{14}$C | mature | 0 |
| Tyrosine-U-$^{14}$C | young | 8 |
| Cinnamic-ring, 3-$^{14}$C | mature | 0 |
| Cinnamic-ring, 3-$^{14}$C | young | 29 |
| Benzoic acid-1-$^{14}$C (ring labelled) | young | 0 |

after elution from the chromatogram with cold ethanol, and the products chromatographed in the butanol/acetic acid/water solvent. Hydroquinone-$^{14}$C was identified by its $R_F$ value and colour reaction, which were the same as those of standard hydroquinone. Arbutin-$^{14}$C obtained from the feeding of glucose-U-$^{14}$C was hydrolysed in the same way to give non-radioactive hydroquinone together with glucose-$^{14}$C.

Phenylalanine-U-$^{14}$C fed to *Grevillea robusta* A. Cunn. was also incorporated into arbutin, confirming the results obtained with pear. In this species, however, the age of the leaf did not appear to be an important factor. In pear, chlorogenic acid was the major compound labelled with carbon-14 obtained when phenylalanine-U-$^{14}$C was fed, but no radioactive chlorogenic acid was obtained with *Grevillea*. According to Bate-Smith, chlorogenic acid does not occur in *Grevillea* (personal communication).

It is not known at present whether tyrosine gives rise to the hydroquinone or the glucose moiety of arbutin or both. It is known to form sugars readily when fed to pear leaves maintained in light.

It is evident, therefore, that hydroquinone may be formed in young pear leaves by the removal of the $C_3$ side-chain of certain phenylpropanoid compounds such as cinnamic acid, phenylalanine, and possibly tyrosine. This, together with the fact that it is not formed from acetate, indicates that it is an aromatic compound formed via the shikimic acid route.

This work is to be published in detail elsewhere.

We wish to thank the National Research Council of Canada for financial support of this project. We also thank Dr. E. E. Conn of the University of California, Berkeley, for a generous gift of ring and 3, carbon-14-labelled cinnamic acid.

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## ENTOMOLOGY

### A Tick infesting the Nostrils of Man

AN interesting example of the necessity for co-operation in the solution of complex problems of tick bionomics was recently brought to my notice by Dr. V. G. L. Van Someren of Nairobi and concerns infestation of the nostrils of man by the immature nymph stage of a tick belonging to the genus *Amblyomma*. These nymphs are white and were removed from the nostrils of three different persons, namely, Mr. D. Van Someren, Dr. V. G. L. Van Someren and Mr. T. H. E. Jackson, during visits to the depths of primary tropical rain forest in Uganda. The two former-mentioned persons were infested while in the Budongo Forest of Bunyoro during July 1952; the two latter while in the Kayonza Forest of Kigezi (known also as the Impenetrable Forest) during May and June 1957. A single example of the same tick was also found by Dr. Van Someren as it crawled up his neck when in the Kibali Forest of Toro.

It is of interest to note that these highly experienced entomologists were never aware of the ticks crawling across their faces or entering their nostrils. The first indication of infestation was tenderness of the nose when touched or when blown. Equally interesting was the absence of irritation or epistaxis and the disappearance of tenderness within a few hours of removal of the ticks. This almost complete absence of reaction to the presence of the parasite in man when acting as alternative host might suggest that nymphs of these ticks normally infest the nasal passages of anthropoid apes (Pongidae). The chimpanzee (*Pan troglodytes* sub. sp.) is in fact common in these Uganda forests.

Examples of these nymphs removed from human nostrils in the Kayonza Forest were examined and compared with all known African *Amblyomma* nymphæ by Dr. Gertrude Theiler of the Veterinary Research Laboratory, Onderstepoort, Transvaal, Union of South Africa, Miss Jane Walker of the East African Veterinary Research Organization, Muguga, Kenya, and by Dr. Harry Hoogstraal, head of the Department of Medical Zoology, U.S. Naval Medical Research Unit No. 3, Cairo, Egypt. Although all three specialists were unable to identify these nostril ticks, it is suggested by Miss Walker that they may be the nymph stage of *Amblyomma paulopunctatum* Neumann, 1899, which in the mature stage is known to be a parasite of the giant forest hog (*Hylochoerus meinertzhageni*) in western Uganda and distributed in equatorial Africa from French Guinea to Uganda.

Anyone hunting in or visiting the Uganda or West African forests could assist the identification of these ticks by examining the nasal passages of mammals, watching for any white ticks falling from the nose of captured chimpanzees or, when aware of nasal tenderness, allowing the ticks to remain *in situ* until engorged with blood and approximately the size of a small pea, when they may become detached and be blown out into a handkerchief or gently removed with forceps. The ticks should not be killed or put in spirit, but should be kept alive in a tin or tube stuffed with moss or moist tissue paper with a piece of rag tied over the top and posted to one of the specialists mentioned above. In man these ticks become attached to the nasal septum or upper anterior recess of the anterior nasal chamber.

I am indebted to Dr. Van Someren for his detailed observations and wish to thank Dr. G. Theiler, Miss J. Walker and Dr. Harry Hoogstraal for examining Dr. Van Someren's specimens.

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## Atypical Spermiogenesis in *Thermobia domestica*, a Thysanuran Insect

Sperm formation of a thysanuran, *Lepisma domestica*, has been repeatedly investigated by a number of workers[1–5]. Unfortunately, diverse opinion prevails on the basic morphology of this sperm.

It is pertinent to recall that Bowen[2] and Nath and Bhatia[3] find *Lepisma* sperm to be unique inasmuch as the funnel-shaped acrosome lies at the posterior and centriole at the anterior end of the elongated nucleus. Nath and Bhatia add further that the mature sperm is devoid of mitochondrial material. On the other hand, Gatenby and his associates, in a number of earlier publications on *Lepisma* and a recent study[6] on another thysanuran, *Pterobius maritimus*, disagree with the interpretatic of Bowen, Nath and Bhatia. In view of these contradictory reports, the present work[7] was undertal n to investigate, employing classical and modern cytological techniques, not only the morphology but also cytochemistry of spermiogenesis in another genus, *Thermobia domestica*. I agree with the assumption of Gatenby and Mathur that the insects (*Lepisma domestica*, *Pterobius maritimus*) and *Thermobia domestica* so closely allied could not have spermatozoa basically different in construction.

The investigations on *Thermobia domestica* confirm the view that thysanuran sperm is atypical in having a funnel-like acrosome in an unusual position behind the nucleus and the centriole at the anterior end of the latter. The identification of the acrosome as a 'post-nuclear' funnel is further strengthened by the observations that it is periodic acid–Schiff positive and that it arises in connexion with the fusion of the dictyosomes. The mitochondrial development is of the usual insect type. Unlike *Pterobius maritimus*, a single rod-like centriole, as observed in the living cells under the phase-contrast microscope, moves around the nucleus, and the acrosome, once deposited on the latter, continues to occupy the basal end of the metamorphosing spermatozoon. Electron microscope study (Fig. 1) reveals, apart from many new features, that the tail flagellum (*AF*) along with the mitochondrial sheath (*MN*) runs adjacent to the nucleus (*N*). This situation can only be interpreted if the centriole from which the tail is always considered to emerge lies at the head end of the developing spermatozoon. The 'lateral fold' of the nucleus in *Pterobius*[6] is most probably the backward continuation of the flagellum.

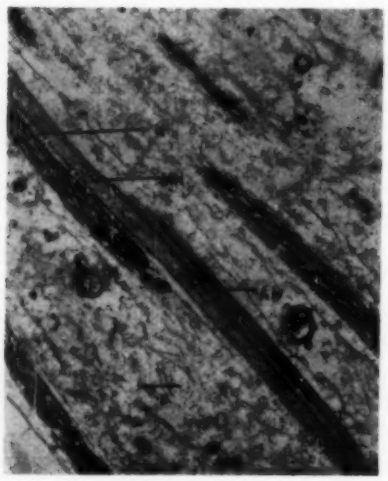

Fig. 1. × 6,000

Most of this work was done as a Boese Post-Doctoral Fellow, Department of Zoology, Columbia University, New York, 27.

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# BACTERIOLOGY

## Germination of Bacterial Spores by Long-Chain Alkyl Amines

Surface-active agents induce striking changes in the physical, chemical and biological properties of bacterial spores[1,2]. The alterations caused by selected quaternary ammonium compounds are relatively minor at room temperature, but rapid and large at 50–100° C. The changes in spores of *Bacillus megaterium* brought about by combinations of mild heat and the quaternary ammonium compounds studied were practically identical with germinative changes induced by L-alanine and inosine[3,4] except that the cells treated with surfactants were nonviable[2]. In all probability this class of surfactants induced germination, the germinated spores being hypersensitive to the concentrations of surfactants required for germination and being killed immediately on germination.

Germinative changes in spores brought about by non-metabolites has been called 'chemical germination' in contradistinction to 'physiological germination'[2,5] effected by amino-acids and ribosides, etc. Germinative changes in spores accompanied by loss of viability (loss of ability to form colonies on agar media) may be regarded as 'lethal germination'.

Chemical germination of spores of *B. megaterium*, whereby germinative changes are accompanied by retention of viability, has now been achieved with long-chain alkyl primary amine surfactants.

L-Alanine, inosine or other physiological germinants are not essential in this system, nor is heat shock[4]. For optimal physiological germination of these spores heat shock combined with L-alanine and inosine or adenosine were found to be essential.

*n*-Dodecylamine [$CH_3(CH_2)_{10}CH_2NH_2$] was added to a suspension of spores of *B. megaterium* (approximately $6 \times 10^7$ spores per ml.) in 0·067 *M* phosphate buffer, *p*H 8·0. Final concentration of the dodecylamine was 0·00006 *M*. The following changes took place within a few minutes at 42° C.: (1) The normally refractile spores lost their refractility as determined by phase-contrast microscopy. (2) The spores became readily stainable with crystal (gentian) violet. (3) The spores were somewhat enlarged. (4) There was a marked reduction in the optical density (at 500–570 mμ) of the spore suspension (Fig. 1). (5) The majority of the cells in the suspension were capable of forming colonies (Fig. 1) on a complete agar medium[2] after neutralization of the dodecylamine with cephalin as described by Baker *et al.*[7]. (6) The surviving cells were not resistant to heat (Table 1). Likewise, they were killed by a variety of physical and chemical stresses which were lethal to spores germinated physiologically, but which were essentially innocuous to normal ungerminated spores (Table 1). (7) The spores lost more than 30 per cent of their dry weight. (8) The spores discharged their dipicolinic acid which appeared in the suspending liquid (Fig. 1). An excretion of calcium and of a peptide which contained hexosamine was also observed. (9) Finally, the spores treated with dodecylamine exhibited an increased respiration at the expense of added glucose; they also had a definite low endogenous respiration. Ungerminated spores had a negligible respiration either in the presence or absence of glucose.

Table 1. Survival of Spores of *B. megaterium* germinated with Dodecylamine

| Stress | Viability (per cent) | | |
|---|---|---|---|
| | Spores germinated with dodecylamine | Spores germinated with L-alanine and inosine | Ungerminated spores |
| None | 100 | 100 | 100 |
| Heated, 20 min. at 65° C. | 1 | 12 | 97 |
| Ultra-violet light, 80 sec.* | 48 | 17 | 89 |
| Freeze–thaw† | 53 | 39 | 98 |
| Ethyl alcohol, 50 per cent‡ | 11 | 12 | 93 |
| Phenol, 1 per cent‡ | 3 | 16 | 95 |
| Hydrogen peroxide, 5 per cent‡ | 18 | 27 | 97 |
| Sodium lauryl sulphate, 0·1 per cent‡ | 8 | 15 | 100 |
| Mercuric chloride, 0·01 per cent‡ | 2 | 14 | 100 |
| Sodium hypochlorite, 0·0005 per cent‡ | 0 | 6 | 96 |
| *p*H 3·3 (HCl)‡ | 35 | 20 | 100 |
| *p*H 11·0 (NaOH)‡ | 38 | 100 | 100 |

* 60 ergs/sec./mm.$^2$.

† Cells were frozen with a mixture of dry ice and acetone and thawed with running tap water in rapid sequence a total of eight times.

‡ Cells were exposed for 2 min. to aqueous solutions of these chemicals, then diluted rapidly and plated to recovery medium.

Since all the above features are characteristic of spores which have been germinated either physiologically or mechanically[8], it seems logical to conclude that true germination took place in the presence of dodecylamine and that this represents chemical germination in the sense described above. Other straight-chain primary amines displayed the germinative properties to varying degrees.

Some preliminary experiments were undertaken to determine whether germination by dodecylamine involves enzymes. Dodecylamine induced a germination-like decrease in optical density, a loss of refractility, a conversion to stainability and a release of dipicolinic acid under the following unphysiological conditions: at an incubation temperature of 70° C., at a *p*H of 11, in a solution containing 10 per cent ethyl alcohol, 15 per cent hydrogen peroxide, 1 per cent phenol or 1 per cent sodium cyanide, respectively. Presumably, any enzymes which might be activated by dodecylamine to elicit the germinative changes would be located near or at the surface of the spore, hence would not only have to persist throughout dormancy of the spore but also would have to be active in all the physiological extremes mentioned above.

The non-enzymatic evidence presented here extends the support[5] for the concept[8] that the prime event in germination is a breaching of a permeability barrier in the dormant spore which permits an ingress of water and attendant rehydration of the vital spore constituents.

A point of major interest now is to determine how the physiological germinants L-alanine and inosine fit into the picture and whether or not they have a function in a non-enzymatic or enzymatic mechanism for rehydrating the bacterial spore.

This work has been supported in part by a grant from the Office of Naval Research.

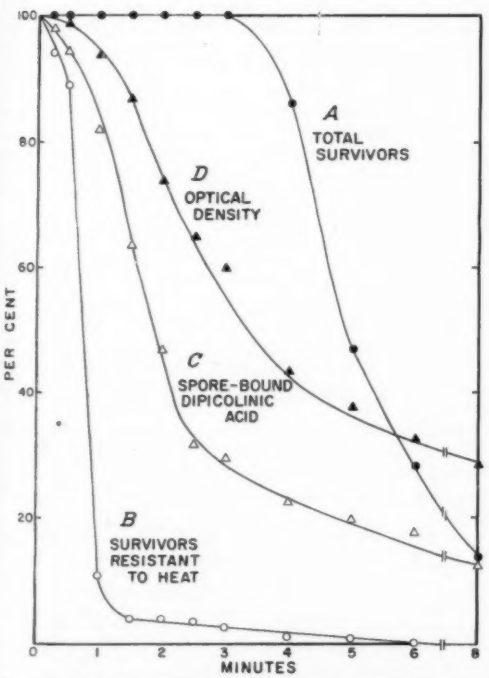


Fig. 1. Chemical germination of spores of *B. megaterium* with 0·00006 *M* dodecylamine, temperature 42° C. Curve *A* denotes survivors which formed colonies on a complex agar medium. Curve *B* denotes survivors which were able to tolerate heating at 65° C. for 20 min. Note that after 1-min. exposure to dodecylamine 90 per cent of the total viable survivors had become sensitive to heat. The dodecylamine was not lethal to the spores until after 3 min. Curve *C* shows that dipicolinic acid gas was released from the spores by dodecylamine prior to loss of viability but at a rate slower than the rate of labilization to heat. Curve *D* shows the typical reduction in optical density which accompanies germinative changes in bacterial spores

An extended account of these and related experiments will be published elsewhere.

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## VIROLOGY

### Polyoma Virus in Syrian Hamsters: a Non-communicable Infection

Epizootics caused by polyoma virus have been reported[1,2] in mouse colonies maintained in proximity to mice infected experimentally with this virus. Establishments without facilities to house infected and uninfected mice in separate buildings run the risk of contaminating their polyoma-free stock. It was of interest to determine, therefore, whether similar problems would be encountered when the Syrian hamster was used as the experimental animal to study this disease. Our experience indicates that infected hamsters rarely transmit polyoma virus to other hamsters or mice. The evidence that polyoma infection is a much less contagious disease of hamsters than of mice is shown by the following experiments.

(1) Hamsters less than 24 hr. old were divided into three groups and injected subcutaneously in the interscapular region with either $10^{4.5}$ mouse embryo tissue culture doses ($TCID_{50}$) of polyoma virus, $10^{2.5}$ $TCID_{50}$, or sterile diluent fluid. The hamsters were appropriately marked and distributed among 13 mothers so that each litter contained 2–4 animals from each group. The hamsters were weaned and placed in separate cages when they reached 21 days of age. Approximately half the hamsters were bled between 41 and 59 days of age. Autopsies were performed on all hamsters dying during the experiment. At 98 days of age the surviving animals were bled, killed and autopsied. The sera were tested by hæmagglutination-inhibition and complement fixation for the presence of antibody to polyoma virus as described elsewhere[3]. As shown in Table 1, there is no evidence that any of the litter-mates injected with sterile diluent fluid contracted infection with polyoma virus.

(2) During assays of tumour-inducing capacity of polyoma virus in hamsters, approximately 200 suckling animals and more than 400 weaned animals were housed at the same time in nursing or individual cages in a single room with a floor area of 900 sq. ft. The hamster cages were arranged in series on long tables according to the age of the animals. To test whether the virus could spread from hamsters to mice, 7 cages each containing 5 young (8–10 gm.) mice were distributed in the room, some adjacent to cages occupied by suckling hamsters recently injected with polyoma virus, some among 21–50-day-old infected hamsters, and others among cages containing infected animals older than 90 days of age. The mice were bled twice, at 40 and 96 days, after being placed in the environment with infected hamsters. During this time all cages were cleaned and changed as needed, and all other usual activities permitted in the room. All the sera of the mice were negative when tested by hæmagglutination-inhibition and complement fixation. Careful gross inspection of the mice killed at 96 days after exposure to infected hamsters failed to reveal the presence of tumours.

Table 1

| Inoculum | No. injected | No. cannibalized before 21 days of age | No. with tumours | No. dead of unknown causes* | No. of animals with antibody : total tested |
|---|---|---|---|---|---|
| $10^{4.5}$ $TCID_{50}$ | 45 | 2 | 24 | 6 | 19/21 |
| $10^{2.5}$ $TCID_{50}$ | 37 | 1 | 10 | 6 | 16/21 |
| Sterile diluent fluid | 35 | 1 | 0 | 4 | 0/20 |

* 14 of the 16 animals dead of unknown causes were dwarfs.

(3) To achieve randomization in experiments with polyoma virus in new-born hamsters, we have distributed our inoculated hamsters so that each litter contained animals injected only with control diluent fluid as well as animals injected with various test dilutions of virus. To date, we have studied nearly 2,500 animals of which 320 were injected at birth with non-infectious materials. From autopsies and serological tests on individual sera it became apparent that only two hamsters injected with non-infectious material at birth showed evidence of infection at the time the experiments were terminated. Although we suspect that they contracted the infection from their litter-mates, we cannot exclude the possibility of error made at the time the inoculum was administered.

Several factors probably account for the non-contagious nature of polyoma infection in hamsters as compared with mice. Mice infected with polyoma virus excrete virus in urine, and cross-infection probably takes place through inhalation of aerosols[1,2]. Hamster urine is considerably less copious, and because of their habits they are less prone to create aerosols. Moreover, virus might be lacking in their urine since polyoma virus multiplies poorly in hamsters albeit tumours are readily induced. This is evident from the finding that only a fraction of tumours induced by cell-free filtrates contain demonstrable virus[3]. Occasionally, hamsters with tumours lack demonstrable antibody[3].

The results indicate that, with minimal care, laboratories doing research with polyoma virus in Syrian hamsters should not have much difficulty in keeping their small animal stock from becoming infected.

This investigation was aided by a grant from the U.S. Public Health Service (*C*-4204).

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# FORTHCOMING EVENT

## Thursday, December 29

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 3 p.m.—Dr. V. E. Cosslett: "Seeing the Very Small". (The One Hundred and Thirty-first Course of six lectures adapted to a Juvenile Auditory. Further lectures on December 31, January 3, 5, 7 and 10.)

# APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER IN ASTRONOMY—The Registrar, The University, Manchester 13 (December 31).

GRADUATE CHEMIST or PHYSICIST at the Houldsworth School of Applied Science, for a two-year programme of research on the physical and chemical properties of clays, particularly those used in the manufacture of building brick and heavy clayware—The Registrar, The University, Leeds 2 (December 31).

LECTURER (suitably qualified science graduate) IN DENTAL MATERIALS, to assist in the teaching of dental students and to undertake research in the physical, chemical and mechanical properties of plastics, elastomers, ceramics, alloys and other materials used in restorative dentistry—The Secretary, The London Hospital Medical College (University of London), Turner Street, London, E.1 (December 31).

RESEARCH WORKER (with some training in physics and mathematics) IN THE DEPARTMENT OF GEOGRAPHY, to assist the Lecturer in Polar Studies in a project concerned with the analysis of heat and water transfer in a river and a glacier basin—The Registrar and Secretary, King's College (University of Durham), Newcastle upon Tyne (December 31).

SENIOR LECTURER IN MATHEMATICS; a LECTURER IN OPHTHALMIC OPTICS; and a LECTURER IN MATHEMATICS OR STATISTICS—The Bursar, College of Advanced Technology, Gosta Green, Birmingham 4, quoting "N" (December 31).

EXPERIMENTAL OFFICER (graduate) IN THE DEPARTMENT OF CHEMISTRY, with responsibility for the maintenance of electronics apparatus—The Registrar, The University, Leicester (January 7).

ASSISTANT (medically qualified for at least three years and interested in human genetics and epidemiology)—The Director, Population Genetics Research Unit, Medical Research Council, Old Road, Headington, Oxford (January 14).

TUTOR (graduate in physics or chemistry or mathematics) IN THE INSTITUTE OF EDUCATION—The Registrar, The University, Hull (January 14).

LECTURER IN COAL PREPARATION IN THE DEPARTMENT OF MINING AND MINERALS ENGINEERING—The Registrar, The University, Edgbaston, Birmingham 15 (January 15).

PSYCHOLOGIST (with an honours degree in psychology or its equivalent) IN THE DEPARTMENT OF SOCIAL ANTHROPOLOGY, to assist in a study of urbanization and the effects of industrialization which the Department is conducting in Sierra Leone, West Africa—Dr. Kenneth Little, Department of Social Anthropology, University of Edinburgh, 3 Buccleuch Place, Edinburgh (January 15).

SCIENTIFIC OFFICER (with at least a good honours degree in geography, with subsidiary zoology and/or botany, or in zoology, with subsidiary geography, and preferably some experience in biogeographical, bioclimatic or ecological research) IN THE GEOGRAPHICAL SECTION, for research in the biogeography and ecology of economically important locusts and grasshoppers—The Director, Anti-Locust Research Centre, 1 Princes Gate, London, S.W.7 (January 16).

PROFESSOR OF MICROBIOLOGY, to take charge of the Department of Microbiology within the School of Biological Sciences, The University of New South Wales—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2 and The Bursar, University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, marking envelope "University Appointment" (January 23).

LECTURER or ASSISTANT LECTURER IN APPLIED MATHEMATICS—The Registrar, The University, Leeds (January 24).

ASSOCIATE PROFESSOR (with a higher degree and preferably specialized in the field of feedback control systems) IN ELECTRICAL ENGINEERING at the University of New South Wales—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2, and the Appointments Section, The University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, marking envelope "University Appointment" (January 27).

SENIOR LECTURER, and a LECTURER IN GEOLOGY at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 27).

BRITISH COKE RESEARCH ASSOCIATION FELLOW (honours graduate in chemistry, physics or applied science relating to fuel technology), to work on the physical chemistry of carbon under the direction of Prof. W. F. K. Wynne-Jones—The Registrar and Secretary, King's College (University of Durham), Newcastle upon Tyne (January 31).

ELDER CHAIR OF PHYSICS in the University of Adelaide, Adelaide, South Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, January 31).

LECTURERS (2) IN PHYSICS at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

LECTURERS (2) IN ZOOLOGY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

CHAIR OF LOGIC—The Secretary of University Court, The University, Glasgow (February 3).

SENIOR LECTURER (with a higher degree or equivalent qualifications) IN PHYSICS at the Newcastle University College, The University of New South Wales—The Agent-General for New South Wales (Dept. HH), 56–57 Strand, London, W.C.2, and the Appointments Section, The University of New South Wales, Box 1, Post Office Kensington, N.S.W., Australia (February 3).

LECTURER IN THE SCHOOL OF MINERALS ENGINEERING—The Registrar, The University, Edgbaston, Birmingham 15 (February 15).

SENIOR LECTURER or LECTURER IN STATISTICS at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, February 15).

CHAIR OF APPLIED MECHANICS tenable in the Newcastle Division—The Registrar, University Office, 46 North Bailey, Durham (February 18).

CHAIR OF PHYSICS tenable in the Newcastle Division—The Registrar, University Office, 46 North Bailey, Durham (February 18).

LECTURER IN PHILOSOPHY at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 18).

IMPERIAL CHEMICAL INDUSTRIES FELLOW IN ONE OF THE FOLLOWING SUBJECTS: CHEMISTRY, BIOCHEMISTRY, PHYSICS, ENGINEERING, CHEMOTHERAPY and related subjects—The Secretary, Academic Council, The Queen's University, Belfast (March 1).

ELECTRONICS TECHNICIAN, to undertake the construction, development and maintenance of electronic and electrical equipment used in the physiological and radiological fields of medical research—The Secretary, Nuffield Institute for Medical Research, 43 Woodstock Road, Oxford.

LECTURER (single man) IN AGRICULTURAL BOTANY (AND ASSISTANT WARDEN)—The Clerk to the Governors, Essex Institute of Agriculture, Writtle, near Chelmsford, Essex.

LECTURER (well qualified, with industrial and teaching experience) IN ELECTRICAL ENGINEERING at the Norwich City College and Art School, Ipswich Road, Norwich—The Director of Education, City Hall, Norwich, NOR 01 A.

LECTURER (with an honours degree and teaching experience, and preferably with higher degrees and evidence of research ability), TO TEACH PHYSICAL CHEMISTRY to B.Sc. General (New Regulations), Grad.R.I.C. and H.N.C. standards—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

LECTURER (with good academic qualifications in mathematics, and either experience of or an interest in numerical analysis) IN MATHEMATICS in the Department of Science, Bournemouth Municipal College of Technology and Commerce—The Chief Education Officer, Town Hall, Bournemouth.

MARINE BIOLOGIST (with a good honours degree in natural science, and preferably experience in marine research) with the Fisheries Development and Research Unit, Sierra Leone, for research into problems connected with the development of the marine and freshwater resources of Sierra Leone and biological investigations designed to assist in the conservation of the trawl fishery—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.65/15/01.

POSTDOCTORAL RESEARCH FELLOWS IN THEORETICAL PHYSICS—L. E. H. Trainor, Physics Department, University of Alberta, Edmonton, Alberta, Canada.

READER (with the qualifications and experience to direct research and postgraduate work, and to take a leading part in advanced teaching) IN PHARMACEUTICS—The Registrar, Bradford Institute of Technology, Bradford 7.

RESEARCH ASSISTANT (suitably qualified in biochemistry, pharmacology or zoology) IN THE WELLCOME LABORATORIES OF PHARMACOLOGY The Gatty Marine Laboratory, St. Andrews, for work on thyroid metabolism of lower vertebrates—The Joint Clerk to the University Court, College Gate, St. Andrews.

RESEARCH FELLOWS and RESEARCH ASSISTANTS (with an honours degree in pharmacy or other allied subjects) IN THE DEPARTMENT OF PHARMACY—The Registrar, Bradford Institute of Technology, Bradford 7.

SCIENTIFIC ASSISTANT (with an honours degree or its equivalent in biological sciences, preferably including physiology; a knowledge of languages, especially Spanish: and the ability to write correct English), to work on literature for *Nutrition Abstracts and Reviews*—The Director, Commonwealth Bureau of Animal Nutrition, Rowett Research Institute, Bucksburn, Aberdeen.

SCIENTIFIC OFFICER (CHEMIST), and an ASSISTANT EXPERIMENTAL OFFICER (CHEMIST)—The Secretary, Room 165(L), New Scotland Yard, London, S.W.1.

SENIOR LABORATORY TECHNICIAN (Grade I)—The Hospital Secretary, Harefield Hospital, Harefield, Middlesex.

TEACHING ASSISTANTS IN THE DEPARTMENT OF CHEMISTRY—Prof. Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

# REPORTS and other PUBLICATIONS

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